THE EFFECTS OF INFLATION, UTILIZATION, PRESCRIPTION SIZE, AND PRODUCT MIX ON PRESCRIPTION DRUG EXPENDITURE CHANGES IN A HEALTH MAINTENANCE ORGANIZATION (HMO)

by

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ABSTRACT

The study goal was to estimate the relative magnitude of inflation, utilization, prescription size, and product mix in prescription claims experienced by an HMO. Claims data for 37,470 prescriptions for continuously enrolled diabetic drug users in five consecutive years were analyzed. All drug products were categorized as ongoing, adopted, abandoned or new entity products. Except for the new entities, they were divided into single-source, multiple-source innovator, and multiple-source generic products, based on types of product sources.

The analysis was composed of two steps. First, a general descriptive analysis was conducted of the total drug ingredient cost, average cost per prescription, average unit price, and average prescription size across the product groups and study periods. Strength mix and therapeutic mix also were identified. Second, Laspeyres, Tornqvist discrete approximation to the Divisia, and refined Divisia indexes were applied to estimate the relative effects of inflation, utilization, prescription size, and product mix.

The total drug ingredient costs increased with diminishing rate across the study years. The ingredient cost of the single-source products had high impact on the total ingredient cost in the last three years, while the ingredient cost of the multiple-source innovator products was a major influence in the first two years. The overall average cost per prescription and average unit price consistently increased across the study periods. The average cost per prescription of the single-source products and new entities were relatively high, compared to other groups. The average unit price of the new entities was relatively expensive. The overall average prescription size consistently increased for all

except the last study periods. The strength mix widely varied across the periods. For therapeutic mix, only biguanides and thiazolidinedione, which had relatively expensive average costs per prescription, had consistent increases in the percentage of prescriptions across the periods.

The indexes showed positive changes for the drug ingredient cost per member per year, except in the last period. The inflation effect was positive for all periods and was the largest effect, except for the first period. Product mix was the most fluctuating effect across the periods, compared to others.

CHAPTER 1

INTRODUCTION

In the United States (U.S.), health care expenditures have been escalating intensively. Recently, they were approximately 13 percent of Gross Domestic Product (GDP) (Health Care Financing Administration [HCFA] 2001). Also their growth seems to be out of control and causing a health care financial crisis. Although health care expenditures are composed of a number of components, drug expenditures are one of the most important factors affecting health care expenditures for several reasons. First, prescription drugs commonly play an important role in primary care. Pharmaceuticals are the most cost-effective forms of medical care and are instrumental in improving the quality of health and well-being (Bobula 1996). In 1998, nearly three billion prescriptions were dispensed in the U.S. (Kreling et al. 2000). Nationally, 65 percent of all physician office visits generate at least one prescription (Hillman et al. 1999). Previously, the growth rate in the number of prescriptions dispensed was approximately six percent in 1995, four percent in both 1996 and 1997 (Levit et al. 1998), while it was more than eight percent in 1998 based on the data presented by Kreling et al. (2000). Second, HCFA (2001) reported that, in 1999, drug expenditures were approximately eight percent of total national health care expenditures, while the hospital care and physician service were approximately 32 and 22 percent, respectively. Even though the amount of drug expenditures has been relatively low compared to hospital care and physician service components, its growth rate has been the highest since 1996. HCFA (2001) reported that expenditures for prescription drugs were $99.6 billion in 1999 and recently have been increasing with double-digit annual growth rates. They projected that the prescription drug expenditures will grow more than 100 percent within 10 years. Third, drug expenditures traditionally have been one of the highest amounts of out-of-pocket cost for consumers among all personal health care expenditures (HCFA 2001). The out-of-pocket payments for physicians and clinical services, and hospital care were approximately $31 and $13 billion, respectively, while it was about $35 billion for the prescription drug out-of-pocket cost.

Several characteristics of pharmaceuticals make their market unique and important. First, physicians who make decisions for drug use neither pay for nor consume drugs. Most patients in the U.S. partially pay for the pharmaceuticals consumed, and the rest is paid by third-party payers, such as government or private insurers. Certainly, the patients ultimately pay as part of a greater pool of insurance beneficiaries and tax payers, but only indirectly (Schweitzer 1997). However, an argument was made that, in the short term, the third-party payers would be forced to increase prescription drug co-payments ("Outpatient Prices Jump" 2000). Second, the drug industry is one of a very few industries that are subject to heavy regulatory controls. The manufacturing, marketing and distributing of drug products are all monitored closely by the government. Third, prescription drugs are one of the fastest area of technological changes. New technologies have an impact on both the supply and demand of prescription drugs. For the supply side, new technologies may be used for formerly untreatable diseases, thus expanding product categories. They may improve providers' ability to treat those patients, diagnose them more completely and earlier and more effectively treat the diseases found (Dubois et al. 2000). New prescription drugs may also affect consumer demand in several ways. For instance, a new drug could reduce the number of sick days, reduce hospitalization, and reduce the risk of old drugs (Lee 1992).

In an era of cost constraints, pharmaceutical companies still produce new products. Research-based U.S. pharmaceutical companies invested approximately $18 billion in Research and Development (R&D) in 1999 and the R&D expenditures were expected to increase 8 percent in 2000 (Pharmaceutical Research and Manufacturers of America (PhRMA) 2001). The most recent estimate of the cost of developing a new drug was $500 million, including the cost of research failures. Also, total drug development time, including approval time, was approximately 14 years for drugs approved during 1990 to 1996. The average effective patent life (post-approval) for new drugs introduced in the 1990s has been only 11 to 12 years. The values of cost and time of R&D show the pharmaceutical industries' effort for the new products. Therefore, the pharmaceutical industry must try to introduce the technologies to the market by manipulating prices, promotion and distribution, so they can recoup their investments. More than 35 percent of prescription drug expenditure in 1998 was for new drugs introduced since 1991 (Foote and Etheredge 2000). Also, pharmaceutical companies have pre-tax net profit margins averaging more than 28 percent, which is almost three times that of other brand-name consumer product companies ("Prescription Sales up 15.4 percent, Price Rate Holds" 1998). However, the technological changes are not only necessarily involved with the introduction of new drugs, but the new generic drugs are also a form of technological changes. These technological changes initiate price changes, which eventually influence the expenditures.

The source of payment for prescription drugs primarily is third parties. In 1999, approximately $65 billion of prescription drug expenditures were third-party payments (HCFA 2001). Lipton (2000) reported that drug costs accounted for more than 10 percent of the medical budgets of health maintenance organizations (HMO) and half of all HMO cost increases. Also, increased drug spending is an important factor in health insurance premium increases. The health care organizations must efficiently manage or create effective policies to control costs. A task of designing policies is that they need to minimize cost or maximize profits, while offering attractive plans to the consumers. Most of the available cost-control strategies focus on the problems at the patient and the provider levels, but not on the manufacturers. An indicator of failure of the cost control strategies is that prescription drug costs still are growing at a high rate, sometimes considered out of control. Recently, rebates from manufacturers have been claimed to compensate for the increases in drug expenditures. However, there also are some limitations. The U.S. Department of Health and Human Services (1995) indicated that the amount of variation in prescription drug expenditure increases was independent of the rebate amount. Therefore, rebate programs may not be complete answers for limiting drug expenditures. Instead, Murray et al. (1998) argued that the rebates increase the use of newer (more expensive) products. Also, McCarthy (1998) reported that drug companies are changing rebate deals based solely on volume and tying rebate amount explicitly to market-share increases. Under the new deals, many of the former rebate collectors will no longer qualify. Prescription drug expenditures recently also became an important political issue that has been discussed very heavily since the government has been proposing Medicare prescription drug coverage. A concern about this new policy is that it will escalate the prescription drug expenditures even more. The issue of factors affecting prescription drug expenditure changes recently has been of interest.

Even though factors influencing the expenditures can be of several types, economically the expenditure has two major components, which are price and quantity. Price factors encompass changes of product prices, type of products used, reimbursement policy, and "aftermarket" arrangements such as rebates from drug companies. Previously, the majority of people believed the increase in drug spending could be attributed to rising prices. What they failed to realize was that increased spending and rising price are not the same thing (Keith 2000). HCFA (2001) reported that the average annual percent change in prescription drug expenditures increased from nearly 11 percent in 1995 to approximately 17 percent in 1999, while the Bureau of Labor Statistics (BLS) (2001) showed that the Consumer Price Index (CPI) for prescription drugs increased from approximately 3 percent in 1995 to nearly 6 percent in 1999. Therefore, prescription drug price explained only a portion of overall prescription drug expenditure changes. The quantity factors basically reflect utilization and are related to the number of users, intensity of use (number of prescriptions per person) and prescription size (units per prescription). Newhouse (1992) did not believe that there was any good empirical basis for decomposing the medical care (including drug) expenditure increase into increases in price and increases in quantity. The high amount of the residual increase is attributable to technological change. Recently, another potential effect was identified (Dubois et al. 2000, Keith et al. 2000, and Express Scripts 2000). This effect is a consequence from the changing of utilization between more or less expensive products. It is called product mix. Product mix effect is neither pure price nor pure quantity effects, but reflects the technological change. The product mix concept is relatively new, compared to the basic concept of price and quantity effects on prescription drug expenditure changes.

In the last two years, several studies identified the factors affecting prescription drug expenditure changes (Barents Group 1999, Ngorsuraches 1999, Suh et al. 1999, DiMasi 2000, Dubois et al. 2000, Keith et al. 2000, Merck-Medco 2000, and Express Scripts 2001). Different definitions and methods were used in these studies. Among these studies, only four studies, which are Ngorsuraches (1999), Dubois et al. (2000), Keith et al. (2000), and Express Scripts (2001) identified the effect of product mix on prescription drug expenditures separate from other factors, while other studies included the product mix effect in other factors. However, none of the four studies showed how to calculate the magnitudes of all effects. Also, the concept of product mix has been confusing. For instance, two groups of researchers from the same health care organization used the different definitions of product mix. This was not only because of different operational definitions, but the concepts were also different. The annual reports of prescription drug trends from Express Scripts defined product mix as changing of utilization between more or less expensive drugs (Express Scripts, 2001), while another research group from Express Scripts defined product mix as cost per dispensed day (Fairman 2000). Apparently, the later definition of product mix, cost per dispensed day, included the effect of prescription size also. Therefore, the previous studies are not applicable for policy makers who want to apply the tools in their organizations. Also, since the calculation was not presented, it is not possible to determine whether the methods used were appropriate or not.

A research question is then, what are the effects of price change (inflation), utilization, prescription size, and product mix on prescription drug expenditure changes? Specifically, the objective of this study is to estimate the relative magnitudes of inflation, utilization, prescription size and product mix changes. This study defines all effects and attempts to apply decomposition methods based on economic index number theory to separate the effects from each other and identify the extent to which inflation, utilization, prescription size and product mix affect or explain expenditure changes. This study is intended to yield insights and perspectives on how key variables can affect the prescription drug expenditure changes.

CHAPTER 2

LITERATURE REVIEW

This chapter will be composed of five sections. The first section will give an overview of previous studies of factors affecting demand and supply for prescription drugs. The second section will provide a review of factors affecting prescription drug expenditures. The third section will give a brief overview of the theory of index numbers, which is the basic concept of the decomposition that will be used in this study. The fourth section will then review the decomposition methods. Finally, the last section will discuss the research significance.

Factors Affecting Demand and Supply for Prescription Drugs

In the U.S., demand and supply for prescription drugs are influenced by five parties, which are consumers, physicians, insurers, pharmacists, and the pharmaceutical industry (Schweitzer 1997). The demand will exist only if the consumer has desire to purchase and the willingness and ability to pay for that product. However, a prescription drug is hardly purchased separately from other health services. Traditionally, physicians act as the patients' agents. They make decisions on behalf of patients. But those who pay for patients' expenses often are third-party payers, both public and private insurers. Then, pharmacists are the ones who actually sell the products in terms of both drugs and related services. The pharmaceutical industry also plays an important role in the drug market. The drug companies not only produce pharmaceutical products, but they also use marketing strategies, such as pricing and promotion, to influence the demand. The following review will summarize studies of factors affecting demand and supply for prescription drugs related to these parties.

Consumers

One of the important aspects of consumers related to prescription drug use is their socio-demographic characteristics, such as age, gender, and race (Schweitzer 1997). In 1988, 34 percent of retail prescription expenditures were used by consumers aged 65 or above, which were only 12.4 percent of the U.S. population (Schondelmeyer and Thomas III 1990). In 1991 the percent of retail prescription expenditures used by this age group was about 35 to 40 percent (Long 1994). Leibowitz et al. (1985) also found that annual drug expenditures varied significantly by age/sex category. Adult women who were more than 65 years old spent twice as much as men the same age. Children, although somewhat more likely than men to have had at least one prescription filled, average only half of men's annual expense for drugs. When outpatient prescription drug claims from the largest of the pharmaceutical assistance programs, the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE), were examined, every major enrollee characteristic, such as gender, race, income, age, residential status, and marital status, was significant in affecting expenditures (Stuart et al. 1991). The Health Insurance Association of America (1999) concluded that one of the factors affecting prescription drug trends was the increasing elderly population. Merck-Medco (2000) examined records for almost one million members who were continuously covered by their pharmacy benefit plan from 1995 and 1999 and suggested that one of the reasons for utilization increases was the aging population. Women proportionately used more drugs and used them for longer periods, but they were less expensive drugs. However, neither spending for prescription drug expenditures nor their trends were significantly different by gender. Momin (2000) compared the variance in the cost of prescription drugs attributable to demographic variables with variance explained by plan characteristics. By using prescription claims data within various therapeutic categories from a Rhode Island-based pharmacy benefit management (PBM) company, differences in average cost of pharmaceuticals among demographic variables were examined after controlling for covariates. Average costs of prescription drugs differed according to demographic variables such as age and gender.

Other than the patient' s age and gender, there are still many variables related to patients' prescription drug use, such as their health status, incomes, and medical preferences. Patients who have poorer health status were found to use more prescription drugs (Coulson et al. 1995, Grootendorst et al. 1997). More frequent and expensive drugs were required to treat elders with several chronic and acute health conditions (Health Insurance Association of America 1999). The income effect was found to be both associated and not associated with prescription drug use. Although Lassila et al. (1996) found that the income effect was not significant, Coulson and Stuart (1995) and Grootendorst et al. (1997) showed that patients with lower incomes used fewer prescription drugs. Ganther (1999) found that medical preferences had a significant effect on prescription drug utilization. Patients with more help-seeking preference used greater numbers of prescriptions and had higher costs of prescriptions.

Physicians

In the agency relationship with patients, physicians are assigned to act or make decisions on behalf of the patients. Fleming (1999) reported that if their doctors assured them a generic drug was as safe and effective as its branded product, 90 percent of patients age 18 or older agreed that it was enough reason for them to use generic products, which were generally less expensive. The demand for prescription drugs has been shown to be associated with physicians' training and experience. Physician years of experience have been shown to significantly and negatively influence costs for antibiotics. Also, physician age significantly influenced costs of prescribed drugs negatively and general practice physicians prescribed drugs lower in cost per day than specialists (Mott and Kreling 1997). However, Hellerstein (1998) examined the importance of physicians in the process by which patients receive either trade-name or generic drugs. Data from the National Ambulatory Medical Care Survey (NAMCS) were used in the study. The observed characteristics of the physicians could not be used to explain why some physicians more likely prescribed more expensive drugs than others.

Hillman et al. (1999) estimated the impact of patient financial incentives on the use and cost of prescription drugs across physician payment mechanisms. A large random sample was selected from members of the United HealthCare Corporation. The results showed that higher patient copayments for prescription drugs were associated with lower drug spending in independent practice association (IPA) models, where physicians were not at risk for drug costs, but have little effect in network models, where physicians had financial risk for drug costs. The results suggested that a way to pace drug spending was to make physicians at risk for the cost of the drugs that they prescribed.

Insurance

There are other studies examining the roles of insurance on the demand for prescription drugs. Most of them focus on various specific sample groups or specific criteria in order to understand particular phenomena, which may be generalized to a broad area. Health care insurers have influenced demand for prescription drugs in many ways. For instance, different cost-sharing strategies developed by insurers affect patient demand for prescription drugs. Insurers also influence the prescribing ability of physicians, such as by developing restricted formularies. In the health insurance market, insurance plans are offered with different cost-sharing options, for instance, coinsurance, deductibles, and copayment.

Changes in prescription drug use resulting from introducing a pre-paid drug insurance program and changes in copayment were reported (Weeks 1973). Prescription drug expenditures per person increased after the copayment was reduced. The effect of a Medicaid drug copayment program on the utilization and cost of prescription services was examined (Nelson et al. 1984). The study concluded that a small copayment (50 cents) for prescription service was a successful mechanism to control the cost and assist in financing a Medicaid prescription drug program. In another study, how cost-sharing affected the use of prescription drugs was investigated (Leibowitz 1985). Individuals with more generous insurance bought more prescription drugs. The results confirmed that expenditures for prescription drugs respond to the cost-sharing faced by consumers. Harris et al. (1990)

determined the effect of different levels of prescription drug copayments on total drug cost incurred for a continuously enrolled cohort of health maintenance organization (HMO) patients under the age of 65 relative to a comparison group that paid nothing out-of-pocket for prescription drugs. The effect of the copayment levels on annual drug costs per enrollee was statistically significant for each copayment level. The copayment levels resulted in higher drug costs per prescription than the comparison group because a relatively larger proportion of more expensive drugs was used. However, lower utilization level in the copayment group offset the increasing cost per prescription and caused lower total annual drug expenditure per enrollee.

Weiner et al. (1991) compared the prescription drug use of persons enrolled in seven prepaid plans to those receiving care in the traditional fee-for-service (FFS) sector. Data for the fee-for-service sector were obtained from a large self-insured employer and data for seven prepaid plans were obtained from the American Managed Care and Review Association (AMCRA). The findings showed that prescription drug utilization rates at each HMO were significantly higher than the FFS rates. The charges per prescription at the HMOs were slightly lower than at the FFS site because the numbers of days of drug therapy dispensed in the HMO prescriptions was higher.

Stuart and Grana (1995) examined the effects of insurance coverage on the selection of over-the-counter and prescription drugs in treating less serious health problems. Data from a survey of Pennsylvania elders who reported suffering one or more of 10 common health problems typically managed with either prescription or over-the-counter medicine were obtained. The results showed that people with prescription coverage more likely medicated a given problem than those without coverage. Given the decision to medicate, the insured significantly used more prescription drugs and significantly reduced the level of over-the-counter use.

Horn (1996) noted that while restrictive formularies were associated with reduced drug costs in some situations, it could be linked with increased use of other services, such as more office visits, more emergency room visits, and more hospitalizations. Martin (1996) examined Medicaid recipients' responses to a decrease in an existing prescription limit. The results showed that, after implementing a five-prescription limit, total prescription use fell 6.6 percent, prescriptions reimbursed by Medicaid fell 9.9 percent, and prescriptions paid for out-of-pocket increased 9.7 percent.

Mott and Kreling (1997) determined whether the therapeutic category of a prescribed drug and patient insurance type influenced the rate of generic substitution and cost saving per generic substitution. New prescriptions were audited from community pharmacies in a Midwestern State. Logistic regression results showed that therapeutic categories for acute conditions were substituted significantly more than chronic conditions and Medicaid prescriptions were substituted significantly more than third-party, indemnity, and uninsured prescriptions. No difference in cost savings per substitution across the insurance types was found. Mott and Rothermich (1998) examined the influence of insurance type, physician characteristics and physician practice systems on the age of dispensed drug products. The results showed that newer drug products were dispensed to patients with prescription drug insurance and with lower out-of-pocket payments.

Motheral et al. (1999) examined the effect of a closed formulary on pharmaceutical use and expenditures, and treatment continuation in a general population of children and adults. Data were obtained from Express Scripts, Inc., an independent pharmacy benefit manager, which implemented a closed formulary in July 1997. A control group, which did not have a closed formulary, was a government plan in the eastern U.S. The results showed that the closed formulary was associated with significantly lower increases in utilization and expenditures, a higher prior authorization rate, and a reduced rate of continuation with chronic medications in the nine months following its implementation, when controlling for age, gender and chronic disease score. The findings suggested that a closed formulary could result in substantial savings to the payer, primarily due to a reduction in the use of brand medications. Then the effect of a closed formulary on pharmaceutical utilization and expenditures in a non-continuously eligible population was investigated (Motheral et al. 2000). Data were obtained from two government employer plans in the eastern U.S. The results suggested that the formulary group had a higher generic fill rate, lower mean total claims per member per month and lower mean brand claims per member per month in the post-period, controlling for age, sex, chronic disease score, and utilization in the pre-period.

HCFA (2000) reported that Medicare beneficiaries who had drug coverage for only part of a year acted like non-covered people during their period without coverage and like other covered people during their period with coverage. The beneficiaries, who had drug coverage for at least 10 months, had a substantial increase in prescription drug utilization. They not only filled more prescriptions than those without coverage did, but they also had access to a broader array of therapies, including more costly therapies. Momin et al. (2000)

compared variance in the cost of pharmaceuticals attributable to demographic variables with variance explained by plan characteristics. Data were obtained from 1996 prescription claims from a Rhode Island-based pharmacy benefit management company. The results showed that plan characteristics contributed to the cost of prescription drugs sixteen-fold, compared to demographic variables.

Pharmacists

Traditionally, pharmacists were expected to provide drugs and tell patients how to use those drugs. More recently, they have become expected to give services, such as monitoring drug interactions, and serve as a source of drug information, and also are required to reduce drug costs by some degree where permitted. (Schweitzer 1997). Moreover, pharmacists are able to reduce drug demand by providing drug counseling, education, and health promotion. Scrivens et al. (1983) suggested that pharmacists may recommend prescription refill, change of medication or dosage, and discontinuation. Talley (1994) reported that pharmacists effectively could manage medication utilization and costs. This was supported by several studies. Britton and Lurvey (1991) showed that the effect of medication profile reviewd by a clinical pharmacist on physician prescribing caused a lower average number of medications and average monthly medication cost per patient. Lobas et al. (1992) examining the effects of pharmaceutical care on medication cost and quality of care in a university-based family-practice clinic. The results confirmed that pharmaceutical care in the ambulatory-care clinic could reduce medication costs and also improve quality of care. Hellerstein (1998) showed that pharmacists substituted generics in approximately half of all cases whenever physicians wrote a new prescription for a trade-name drug, where a generic was available. Meindl et al.

(1998) examined the impact of a clinical pharmacist in an internal medicine clinic on drug utilization. A pharmacy consulting service helped assist physicians with medication management, provided therapeutic regimen reviews, and provided patient counseling. The activities changed drug utilization levels in the clinic and incurred medication cost savings. Recently, Creixell et al. (2000) also examined pharmacists' clinical responsibilities to ensure the rational use of antimicrobial agents and found a decrease in antibiotic use was achieved when the pharmacist's intervention was completed.

Industry

Prescription drug expenditures are also connected to the pharmaceutical industry, which is a supplier. The pharmaceutical industry is different from other industries because of its marketing conditions, such as a consumer-agent relationship directing demand. The pharmaceutical industry marketing efforts are not specific to only patients, who directly consume pharmaceuticals, but also to other components of the prescription drug market, for instance, providing information or advertising. The role of pharmaceutical manufacturers was defined as discovering new drugs, rapid and safe development of these drugs into useful therapeutic tools, and production and distribution of safe and efficient existing drugs (Smith 1991). A primary role of the pharmaceutical industry is research and development of new drug products (Schweitzer 1997). Therefore, pharmaceutical companies face costs resulting from their research and development, plus costs of production and distribution of the resulting products. Also, there is a large number of firms in the pharmaceutical industry, thus they have to compete with each other for market share given purchasers' budget constraints.

The principle pressures on pricing that face pharmaceutical manufacturers have been illustrated (Moore 1997). These included research and development costs, sales and marketing costs, and government controls. Therefore, the pharmaceutical industry tries to introduce products to the market. To support this, a study confirmed that two missions of the industry were to facilitate the treatment of patients with prescription medicines that were effective, safe, and efficient, and to generate sufficient profits to survive and to innovate in an increasingly competitive environment (Jackson 1992).

Manufacturing and promotion were noted as important factors for pricing policies of the pharmaceutical companies (Monaghan and Monaghan 1996). Increasing research and development expenditures, eroding patent lives, and increased competition are factors affecting the future of the pharmaceutical industry. PhRMA (2001) reported that research-based pharmaceutical companies invested approximately $18 billion in Research and Development (R&D) in 1999 in the U.S. and the R&D expenditures were expected to increase 8.03 percent in 2000. One of the essential mechanisms for encouraging pharmaceutical research and development is the protection of intellectual property pertaining to new drugs by the patent system (Schweitzer 1997). In the U.S., new drugs can be legally protected for up to 20 years from the date of filing by obtaining a patent from the federal government. However, the expiration of patent protection on the original compound may not be an informative indicator, because monopoly profits while the patents are active induce competitors to develop and introduce imitative drugs. Even though these are not identical in molecular structure and mechanism of action to the original new molecular entities, they may share some parts of the market. This can have a number of implications for price. For instance, companies may price as high as possible for the exclusivity period, which is the period between the first product to be launched in a particular class and the imitative products which follow, and then drop the price in line with competition when competing products appear (Moore 1997). A second approach would be that companies may launch with a low price to gain as much of a market as possible before competitors arrive, and then attempt to hold on to this market. A third option is that companies may launch at a reasonably high price and attempt to maintain this when competition arrives, assuming that the first product available to consumers is superior to others.

Certainly, innovative products eventually can experience generic competition when their patents expire. Some products may not experience generic competition for many years after the patent expires, either because of delays in FDA approval of generic copies or because the total market for the drug is too small to induce generic manufacturers to enter the market. The effect of patent expiration and subsequent entry of generic drugs into markets for innovative pharmaceuticals that lost their patent protection during 1976 to 1987 were examined (Caves et al. 1991). The results suggested that the price of branded drugs tended to increase in the period between patent expiration and entry of generic products. Then the innovator's price declined with the number of generic entrants, but the rate of decline was small, falling roughly two percent after the first entry but only 22 percent with twenty generic competitors. The overall impact did not statistically significantly lower the prices of branded products. However, Berndt et al. (1996) tracked the price of antidepressant prescription drugs, and found that manufacturers tended to increase the price of branded products after generic entry, apparently concentrating on the price inelastic market segment and letting the generics gain market share from the elastic segment. In another study, price trends were compared before and after patent expiration of thirty-five chemical entities, whose patents expired during the period from 1984 through 1987. The rates of price increase for the originator after patent expiration were higher than before patent expiration, but they were not significant (Suh et al. 1996).

Besides price, promotion is another strategy used for maximizing the value of products both before and after patent expiration. Promotion is claimed to be a mixture of information and persuasion. Promotion's main objectives are to generate product awareness, to create a brand image, to supply information regarding benefits and superior features of the brand, and to combat competitive claims (Smith 1991). John (1994) found that advertising could play a major role in determining the sales and market shares of two products. Vitry (1996) showed advertising intensity increased prescribing habits of physicians, and that familiarity with the advertisements encouraged positive attitudes toward ongoing prescribing at the same or at a higher frequency. During the various stages of the product life cycle, different advertising strategies may be applied with special consideration for generic competition. As a patented drug product is introduced into the market, pharmaceutical manufacturers will attempt to inform and persuade providers to prescribe their new products, while the advertisements after patent expiration imply competition between brand-name and generic drug products (Taylor et al. 1995).

Caves et al. (1991) found the branded product quantity sold fell after the patent expired, with the lower prices offered by generic entrants failing to compensate for the demand contraction. Another reason apparently was the branded producer's reduction in advertising expenditures. The branded producer accumulates loyalty-inducing goodwill during the period of patent protection. Then there is a marked decline in promotional activity prior to patent expiration and generic entry, because a large share of promotional activities by the branded producer would have positive spillovers to generic producers.

Historically, most sales promotion techniques focused on health care providers, because they almost always were the ones who made decisions for drug uses. Recently, direct-to-consumer (DTC) advertising has been applied in the market. A study examined consumers' purchasing decisions for prescription medication (Fahey 1996). One-half of respondents reported they considered pharmaceutical advertisements as educational, helping them become more informed consumers. A number of pharmaceutical companies have turned to direct-to-consumer advertising to ensure that their products' names become familiar to and valued by consumers (Denitto 1993).

There has been considerable discussion about the issues of DTC advertising of prescription drugs. Pharmacists' attitudes toward DTC advertising of prescription drugs were determined (Duttagupta et al 1994). Their results revealed that more than half of respondent pharmacists did not support DTC advertising. Consumers requested that pharmacists provide drugs that were advertised through DTC advertising. Increased advertising costs related to DTC advertising would cause higher drug prices for consumers. Certainly, drug promotion cannot only cause higher drug utilization, but it also increases costs for the pharmaceutical industry. Eventually, drug advertising becomes a significant amount of the cost of marketing a drug and an important component of the pricing formula. In 1999, Health Insurance Association of America agreed that one of the factors affecting prescription drug trends was direct-to-consumer advertising. The Barents Group (1999) examined price and utilization drug data from Scott-Levin Company's Source Prescription Audit database for 1993 and 1998. They showed that one area of major spending growth was found in a few therapeutic categories, which included heavily advertised drugs. In fact, the 10 most heavily promoted drugs in 1998 shared over a fifth (22%) of the total growth in prescription drug expenditures between 1993 and 1998. Recently, HCFA (2000) also concluded that a factor related to increased demand might be greater consumer awareness of therapies because of the growth of DTC advertising for prescription drugs. Wilkes et al. (2000) reviewed previous studies about the impact of DTC advertising of prescription drugs. DTC advertising clearly was concluded to increase the volume of prescribed drugs.

Up to now, some effects of both demand and supply side factors on price and quantity of prescription drug use in the market have been discussed. Recently, another important factor of price and quantity changes is the relationship between managed care and the pharmaceutical industry. The relationship between the pharmaceutical industry and managed care in the marketplace in regards to how this relationship has an impact on drug expenditures has been discussed (Cohen 1996 and Genuardi et al. 1996). The concept of managed care was applied to the prescription drug industry in the mid to late 1980s. While the pharmaceutical industry historically was confronted with the traditional parties, such as physicians, hospitals, and pharmacists, it began to deal with managed care organization (MCOs), such as health maintenance organizations (HMOs), preferred provider organizations (PPOs), and pharmacy benefit managers (PBMs). As mentioned before, these managed care organizations use a number of methods to control pharmacy costs for insured groups.

Recently, the increased role of managed care in pharmacy benefits led to the use of rebates. Pharmaceutical firms pay rebates to PBMs and other MCOs when their products are given preference on the formulary. The pharmaceutical industry has two characteristics easily pressured by managed care. First, there are many brand-name drugs, which can be substituted for others in the same therapeutic class, including generic drug competition. Second, the fixed costs of the pharmaceutical industry related to research and development and smaller marginal production costs make it worthwhile for the industry to pay rebates to those insurers capable of shifting market share. The rebate program has become more ambiguous because of a strategy involving the manufacturer getting into the disease management business by either buying a pharmacy benefit management company or starting one of its own (Tindall 1996). One study examined the impact of the Medicaid drug rebate program on expenditures, utilization, and access via a nationwide study (U.S. Department of Health & Human Services 1995). After adjusting for rebates and enrollment growth, seven of the eight usable case study states had less than seven percent increase in expenditures over a two year period. For these seven states, this increase was equal to, or less than, the general rate of inflation. However, the observation suggested that the amount of variation in expenditure increases was independent of the rebate amount.

In conclusion, the prescription drug market is unique in part because it is composed of several main parties, such as patients, physicians, insurers, pharmacists, and the pharmaceutical industry. All components have their own roles and can change quickly. There also are interactions between parties that can yield more effective utilization, including to control increasing cost. The dynamic roles of these parties consequently will influence different effects on the prescription drug expenditures, such as price, prescription size, utilization, product mix, and new products, which will be discussed as follows.

Factors Affecting Prescription Drug Expenditures

Several studies have examined the factors affecting prescription drug expenditures. Table 2.1 summarizes the conclusions from some of the previous studies. According to these studies, the factors affecting prescription drug expenditures include inflation, utilization, prescription size (unit per prescription) and product mix. However, many the studies included only conclusions, and did not show the methods that were used for capturing the factors.

Research scientists from Express Scripts have followed drug trends through the 1990s (Express Scripts 2001). Also, in 2001, prescription medication trends in 2000 for a large sample of Express Scripts, Inc. clients were examined. Prescription drug growth rate was analyzed in terms of per member per year Average Wholesale Price (AWP) ingredient cost changes. It was primarily composed of three components, which were changes in the utilization of "common drugs", which were available medications for use between 1996 and 2000, increases in ingredient cost per prescription of these common drugs, and the introduction of new entities to the market. Consequently, the prescription drug growth rate was broken down into six factors, which were unit price, units per prescription, strength mix, therapeutic mix, utilization, and new entities. Of the change in common drug costs between 1999 and 2000, 5.4 percent was attributable to the inflation rate for common drugs, 1.0 percent for the units per prescription changes, 0.9 percent for strength mix, 4.2 percent for

Table 2.1 Summary of Studies of Prescription Drug Expenditure Changes

Studies	Conclusions
1. Gagnon et al. (1975)	Two variables, frequency of administration and quantity prescribed, were the greatest influencing factors on the cost of prescription drugs..
2. Firestone (1979)	During 1960 through 1978, the rise in prescription costs was not only the result of higher prices for drugs, but also the mix of prescribed products, such as a more or fewer proportion of prescriptions for lower-priced drugs, the number of doses prescribed, and the introduction of new entities.
3. Nyman et al. (1981)	The increase in prescription cost followed the recent commercial availability of several new antineoplastics (relatively high unit costs, and non-substitutable nature). Only a small part of the increase in costs was attributed to increased inflation.
4. Nelson et al. (1984)	Increasing drug expenditure was attributed to inflation in the cost of ingredients rather than an increase in average prescription size.
5. Karl et al. (1989)	Not only prescription charges but also quantity changes drove the prescription drug expenditures.
6. "A Bitter Pill To Swallow" (1990)	The high prices of new drugs led to inflated prescription drug expenditures.
7. Schondelmeyer and Thomas III (1990)	Inflation (the average price per prescription) was the major force contributing to increased expenditures in the Medicaid drug program between 1982 to 1988.

8. "Rx Goes Control Beyond Plan Design" (1991)	Inflation, increased utilization, and use of newer, more expensive drugs increased the prescription drug expenditures.
9. Glaser (1992)	Parts of the reasons of unsuccessful cost controls were population and inflation effects.
10. Kotzan et al. (1993)	After controlling quantities of supplied doses of H2-antagonist drugs, the total drug cost reduction was found. The quantity of drug used was a significant component of drug expenditures
11. McKnight (1993)	A potential factor affecting changes of prescription drug expenditures was price inflation.
12. U.S. Department of Health and Human Services (1995)	The growth in Medicaid drug expenditures from 1988 to 1993 was attributable to a number of factors, such as drug product price changes, and changes in numbers of prescriptions per user (intensity). The differences in drug product mix contributed to some differences in the price changes.
13. Johnson et al. (1997)	Per capita antidepressant costs increased largely because of the high cost per unit of SSRIs.
14. Levit et al. (1998)	Prescription drug spending increased at high rates during 1995 and 1997 because of the large number of new, higher-price drugs entering the market, and an increase in prescriptions filled.
15. McCarthy (1998)	The main factor of the current pharmacy expenditures is increased utilization.
16. Smith et al. (1998)	Almost the entire recent high drug expenditure growth is accounted for by increasing utilization (number of prescriptions) and intensity

	(including changes in size and mix of prescriptions).
17. Glaser (1999)	A primary reason for the price expansion is the adding of new drugs into the market.
18. Health Insurance Association of America (1999)	New drugs released after 1992 were only 16.8 % of total 1997 utilization, but were 30.6 % of total 1997 costs.
19. Berndt et al. (1996)	Treatment expenditures (including antidepressants) for depression have increased since 1991 because of volume (quantity) increases rather than price increases.
20. Greenberg et al. (2000)	An attribute of the increases in prescription dug expenditures was the high cost of new drugs.
21. Mullins et al. (2000)	Between years 2000 and 2004, the increase in total drug spending was projected to be attributed to prices rather than utilization. Also, the cost increase will come as new drugs replace older drugs for current users.
22. Pharmaceutical Research and Manufacturers of America (2000)	According to data from IMS Health, the main factors of prescription drug sale growth in the late 1990s have been non-price factors, such as increased volume of prescriptions, sales of new products and new product formulations, and the changing mix of available products being used.

therapeutic mix, and 3.7 percent for utilization of common drugs. New drugs accounted for 0.3 percent of the overall per member per year AWP ingredient cost change. The percentage changes do not add up to the changes of total cost per member per year, which was 16.2 percent, because the calculation was multiplicative. The calculation procedure was very briefly noted. Therefore, it is difficult to understand and apply their method as a replication study. Also, price changes were calculated at the chemical entity level, not National Drug Code (NDC) level. The price changes would more likely show smaller increases in the cost of products, which had generic versions available.

The Barents Group (1999) found that the factors underlying the increases included changes in utilization of existing products in the market, increases in the price of existing products, and the introduction of new or improved products. The prescription drug price in this study was the average price per prescription, calculated by dividing total expenditures for the drug by its total number of prescriptions. The new products included all products launched in 1992 or after, instead of the introducing year as did Express Scripts. This allowed the diffusion period for the new products to become more established and cause significant sales volume. The results showed that the prescription drug spending increased because of both higher prices and increased utilization. During the study period, 64 percent of the increases in drug expenditures was attributable to higher drug prices, and 36 percent to increased utilization. The price effect of older drugs accounted for 22 percent and the price effect of new products was 42 percent. The utilization effects of older and new products were only 13 and 23 percent, respectively. Since the price factor was determined in terms of average cost per prescription, it thus included dosage and prescription size effects too. This study did not identify the effect of product mix or others separate from the effects of average cost per prescription and utilization.

Ngorsuraches (1999) examined the relative magnitudes of effects of price change and product mix on prescription drug expenditures from 1995 to 1997. Prescription claims data from an HMO were analyzed. The anti-ulcer drug group was selected for examination. The average cost per prescription, utilization, strength mix and therapeutic mix also were determined. The concept of index number was introduced to separate the effects of price and product mix. However, the study suffered from the fact that the quantity index number used incorporated both utilization and product mix together.

Suh et al. (1999) proposed a study equation to examine factors contributing to national Medicaid drug expenditures between 1990 and 1995. The study equation included price and drug use variables, which were inflation, number of people receiving prescription drugs, more prescriptions written per individual and growth in residual. The inflation was determined by average prescription price. The results showed that overall prescription drug price increased 66.6 percent, population growth was 13.4 percent, the growth in numbers of prescription per capita was 50.2 percent, and the growth in intensity was -30.1 percent. Since the growth of prescription drug prices was measured as the increase in the average price of a prescription drug, this study suffered the same bias on the price factor as the Barents Group study (1999) did. The residual was defined as real drug expenditures, and termed as intensity. It was the combined effects that could not be measured or differentiated individually. It included the effects of the introduction of new drugs and changes in prescription drug usage. In other words, the product mix effect was not separated yet.

Thomas (2000) examined the dynamics of medication use over time in a fixed population. The study intended to observe the treatment strategies, changing use patterns as new drugs were introduced and also the extent to which the growth of the medication classes representing substitution from older drugs or greater numbers of people treated. Prescription claims data for the years 1996 to 1999 provided by PCS Health System, Inc. were examined. Only members, who continuously enrolled during 1996 and 1999, were examined. This allowed the study to identify the new and increasingly prescribed medications and to illustrate different important aspects of expenditure growth and treatment changes over time. The increased annual cost per enrollee was decomposed into three components, which were price, utilization and their interaction. The price factor was determined by cost per prescription changes, and the utilization was defined as number of prescriptions per enrollee changes. Only three treatment categories, gastrointestinal disease, arthritis and pain relief, and high cholesterol, were chosen for study. Different relative contributions of price versus quantity across categories were found. Even though the study did not separate the product mix effect from the price and utilization effects, it provided the idea of fixing the continuous enrollees, which let the study reflect the effect from the product behavior, not from enrollee mix.

Dubois et al. (2000) also examined the factors contributing to prescription drug growth. The prescription claims data for the highest spending or the fastest-growing drug categories reported in other studies were examined. The data were retrieved from two sources, which were 1995 and 1998 data from Protocare Sciences' databases, and 1994 and 1997 data from MEDSTAT's MarketScan databases. Factors contributing to prescription drug spending growth were computed using a multiplicative growth equation, where the product of the individual growth factors equaled the overall growth rate in spending per health plan member. Total spending growth for each drug category was decomposed into several price and volume factors. Price factors were defined as those affecting the price per day of therapy and volume factors were defined as those affecting the intensity of use and the number of users. The study was conducted with individual NDC numbers as the level of analysis. Two price factors, which were inflation and the change in strength and therapeutic mix, were calculated for the NDCs available in both the base and comparison years. Two volume factors also were calculated, changes in the number of prescriptions per person and the number of days supplied per prescription. The concept of Consumer Price Index (CPI) was used to measure inflation. One price and two volume factors were computed to capture the impact of new NDCs in terms of changes in the average price per day, the number of prescriptions per person, and the number of days per prescription. Another volume factor was the change in the number of users and potential users of prescription drugs per thousand plan members. Volume, not price, was found to mainly drive the drug spending growth. Even though the concept of a mutiplicative growth equation was described (the method of the separation all factors), the calculation procedure was still unclear, especially for product mix.

Merck-Medco (2000) reviewed the records for almost one million members who were continuously covered by their pharmacy benefit plan from 1995 and 1999. The prescription drug spending was determined by the average cost per member per year. The cost increases were broken down into three components, which were the number of users change, the increase in days per user, and the increase in drug cost per day. The results showed that the average cost per member per year increased 113 percent between 1995 and 1999 with an average annual rate of 20.6 percent. Each component of the cost increases accounted for approximately one-third of the overall increase. The study used continuous enrolled samples, which revealed the results from products used rather than the results from enrollee mix. However, the method used for calculation was not mentioned. Also, the increases in cost per day included both drug mix and inflation. Therefore, there was no separation between product mix and price effects.

Chernew et al. (2001) decomposed pharmaceutical cost growth into price and quantity components and also compared growth across different types of health plans. Pharmaceutical claims from a national employer between 1996 and 1998 were analyzed. Price effect was defined as dollars per prescription and was captured by a proposed price index. The quantity measure was number of prescriptions and a quantity index was calculated. The quantity index was further divided into growth-in-prescription index and a mix-of-prescriptions index. Pharmaceutical spending growth was found primarily attributable to changes in utilization as opposed to price changes. The utilization changes also were found to be complex and differed across types of health plans. Even though the study was an application of the decomposition of drug expenditure changes, the decomposition method was still problematic because the price index, measured as price per prescription, in the study still included product mix effect. This might lead the study to underestimate the changes in the mix of prescriptions.

In conclusion, even though there have been several studies regarding factors affecting prescription drug expenditures, none of them provided clear methods or calculations in the reports. Also, some of them did not separate each individual factor from each other. For instance, some studies included the product mix in the price effect or some studies included the product mix in the effect from the quantity change. Additionally, the results from the studies that did not examine the continuous enrollees might have experienced a change of enrollee mix during the study period. Therefore, various features of the methods of calculation can be improved and clearly presented.

Theory of Index Numbers

Since the theory of index number will be applied in this study, this section will briefly provide general information about index numbers including previous studies. The review will highlight some literature, but a thorough review is beyond scope of this study.

If there were only a single commodity in the market, the changes in its price and its quantity would indicate expenditure changes. But there are a lot of commodities in the market, and each item may have a different change. Indexes are a way to present the price and quantity changes. The theory of index numbers has been used both domestically and internationally to determine price indexes, as economic indicators (Allen 1975).

Index numbers have a long history. The classical definition of index number was stated in the nineteenth century in Britain by Edgeworth (Allen 1975):

> "I propose to define an index-number as a number adapted by its variations to indicate the increase or decrease of a magnitude not susceptible to accurate measurement."

Even though there are many types of indexes, the Inter-Secretariat Working Group on National Accounts (1993) concluded each price index is based on an average of proportionate changes in the prices of a specified set of goods and services, while each volume index is an average of proportionate changes in the quantities of a specified set of goods and services. The index number generally compares two time periods. In economic practice, index numbers come in pairs, one of price and the other a matching one of quantity. Basically, the period selected as the reference point will be assigned as period 0 and the compared period will be assigned as period t. These two periods must be separated. The ratio of the price, or quantity of a product between period t and period 0 is defined as a price relative or a quantity relative. Ordinarily, they are expressed with one selected situation as 100, because index numbers measure changes. To average the change, either a stochastic approach (unweighted) or aggregative (weighted) approach can be used to calculate the index number (Allen 1975). However, the weighted approach is the one that generally is used to calculate economic indexes, because it provides more economic sense. The aggregative/weighted approach contains several forms. Only some forms, such as base-weighted and current-weighted indexes, which are fundamental indexes, will be discussed.

Laspeyres and Passche indexes are defined as weighted averages of price and quantity relatives, the weights being the values of the individual goods or services in one or other of the two periods being compared (Hill 1993). Laspeyres price index (Lp), a well-known base-weighted index, is defined as a weighted arithmetic average of the price relatives using the values of the earlier period 0 as weights, whereas the Laspeyres quantity index (Lq) is defined as a weighted arithmetic average of the quantity relatives. The period that provides the weights for an index is the "base" period. Algebraically, the Laspeyres price and quantity indexes are as follows;

$$Lp = \sum P_t Q_0 / \sum P_0 Q_0$$

$$Lq = \sum P_0 Q_t / \sum P_0 Q_0$$

Therefore, the basic Laspeyres forms are interpreted as the changing expenditure on the fixed Q_0 quantity (price index) or the changing expenditure at fixed P_0 price (quantity index). It is noteworthy that the Laspeyres price index implies a zero substitutability assumption. In other words, the goods are assumed to be completely nonsubstitutable. The concept of Laspeyres index is used as a fundamental of the Producer Price Index (PPI) and Consumer Price Index (CPI), which will be mentioned later.

Passche price index (Pp), a current-weighted index, is defined as a harmonic average of the price relatives using the quantity values of the later period t as weights, whereas the Passche quantity index (Pq) is defined as a harmonic average of the quantity relatives. Algebraically, the Passche price and quantity indexes are as follows;

$$Pp = \sum P_t Q_t / \sum P_0 Q_t$$

$$Pq = \sum P_t Q_t / \sum P_t Q_0$$

The Passche index can be interpreted as the reciprocal of a "backward looking" Laspeyres, which is the reciprocal of a Laspeyres index for period 0 that uses period t as the base period.

An ideal, which combines both information from Laspeyres and Passche indexes, is called Fisher's ideal index. Fisher's ideal index is defined as the geometric mean of the Laspeyres and Passche indexes, which are

$$Fp = (Lp*Pp)^{0.5}$$

$$Fq = (Lq*Pq)^{0.5}$$

where Fp and Fq are Fisher's ideal price and quantity indexes, respectively. However, the Fisher's index is not easy to interpret.

Since the basic idea of the Laspeyres and Passche indexes is based on a fixed year, it tends to be less relevant to the economic situation of later periods. This problem can be solved in several ways. One of them is the concept of a "chain index", which will link the indexes between consecutive periods together and will measure the actual movements of price and quantity from period to period.

Chain Index Number

The concept of this type of index is changes in prices and quantity between periods that are separated in time are obtained by cumulating the short-term movements (Allen 1975, Hill 1993). The chain index has a number of theoretical advantages, for instance, it is possible to obtain a much better match between products in consecutive time periods than between periods that are far apart, thus new products or new qualities can be added continually.

The Divisia Integral Index, a basic concept of chain index number, was defined as a price or quantity index varying continuously over time (Allen 1975). The continuous price index P(t) or quantity index Q(t) is defined and expressed by

$$P(t) = P_0\, e^{f(t)}, \text{ where } P_0 = 100 \text{ in base year } 0$$

$$f(t) = \int_0^t \phi(t)dt = \ln P(t) - \ln P_0$$

where

$$\phi(t)dt = d\{\ln P(t)\} = dP(t)/P(t) = \left(\sum_{i=1}^{n} q_i(t)dp_i(t)\right)/\left(\sum_{i=1}^{n} p_i(t)q_i(t)\right)$$

and p_i, q_i are price and quantity of each commodity (i = 1, 2, 3, 4,.....,n), respectively.

By definition, it needs continuous price and quantity data for all commodities. Therefore, it requires a practical approximation, which is applicable to the discrete time intervals to which actual index numbers relate. Several methods were used to approximate the continuous price and quantity data for all commodities. Therefore, they created different types of Divisia indexes.

An example of the continuous Divisia index is the chain Laspeyres price index (L_p^c) (Allen 1975). The chain Laspeyres index is based on annually linked Laspeyres indexes. The link connects the index from year t to (t+1). Algebraically, the chain Laspeyres price index is as follows;

$$L_p^c = (\Sigma P_1Q_0/\Sigma P_0Q_0)\ (\Sigma P_2Q_1/\Sigma P_1Q_1)\ldots(\Sigma P_tQ_{t-1}/\Sigma P_{t-1}Q_{t-1})$$

The interpretation of the chain Laspeyres index is thus the index in year t comprises a sequence of t separate links, each representing the changing cost of a fixed budget. The budget is fixed at the start of each year and is changed from year to year. It provides the advantage that the base is brought constantly up to date. The United States Department of Labor's Bureau of Labor Statistics (BLS) uses these indexes as a basis for developing the measures of price inflation (Berndt et al. 1996).

Another well-known Divisia index is the Tornqvist discrete approximation to the Divisia price or quantity index (Hulten 1973 and Theil 1973). As mentioned above, the continuous Divisia index needs a practical approximation, which is applicable to the discrete time intervals to which actual index numbers relate. The Tornqvist discrete approximation frequently is used for the Divisia index (Diewert 1978).

Let I_t^T be the Tornqvist discrete approximation to the Divisia price index. Algebraically, the Tornqvist discrete approximation to the Divisia price index is presented as follows (Triplett 1999);

$$\ln(I_t^T / I_{t-1}^T) = \sum_{i=1}^{n} \overline{w_{it}} \ln(p_{it} / p_{i,t-1})$$

where

$$\overline{w}_{it} \equiv (w_{it} + w_{i,t-1})/2$$

and

$$w_{it} \equiv (p_{it}q_{it})/\sum_{i}^{n} p_{it}q_{it}$$

and p_{it}, q_{it} are price and quantity of each commodity (i = 1, 2, 3, 4,…..,n), respectively, at time t. The Torqvist discrete approximation to the Divisia index also is applied to create a quantity index.

The Sato-Vartia index number is another type of Divisia index. Sato (1976) found a log-change index number and it was used particularly as an approximation to the theoretic Divisia index by using a logarithmic mean weight instead of using the arithmetic mean weight formula. Let I_t^{SV} be the Sato-Vartia price index. The formulae become

$$\ln(I_t^{SV} / I_{t-1}^{SV}) = \sum_{i=1}^{n} \overline{w_{it}} \ln(p_{it} / p_{i,t-1})$$

where

$$\overline{w_{it}} = \{[(w_{it} - w_{i,t-1})/\ln(w_{it}/ w_{i,t-1})]/ \Sigma[(w_{it} - w_{i,t-1})/\ln(w_{it}/ w_{i,t-1})]\}$$

and

$$w_{it} \equiv (p_{it}q_{it})/\sum_{i}^{n} p_{it}q_{it}$$

and p_{it}, q_{it} are price and quantity of each commodity (i = 1, 2, 3, 4,…..,n), respectively, at time t. These formulae also are applied to create a quantity index.

The Relationship among Index Numbers

Index numbers commonly are used to summarize economic information about a bundle of commodities. They can be applied to several economic functions such as cost function, profit function, and expenditure function. However, to calculate the exact index numbers or theoretic indexes to these functions, the function to be indexed needs to be identified. Generally, the Laspeyres index tends to be a larger increase over time than the Passche index (Hill 1993). This relationship holds whenever the price and quantity relatives are negatively correlated which is usual in general cases. Hill (1993) also concluded that the Laspeyres and Passche indexes typically provide an upper and lower bound to the corresponding economic theoretic index, respectively. The Tornqvist approximation to the Divisia price or quantity indexes is an example of the exact index number when the function to be indexed is a translog function (Diewert 1978, Lau 1979, and Hill 1993). The Torqvist approximation to the Divisia index also is called a superlative index number, which is a true index number associated with a flexible functional form (a function which does not impose a priori assumption on the elasticity of substitution) that is a translog function in this case. This also allows the Torqvist approximation to the Divisia index to need no priori assumption about the elasticity of substitution among commodities (Triplett 1999). The Fisher's ideal index also is an exact and superlative index number. The Fisher's ideal index is an exact index if and only if the function is the square root of a quadratic function (Lau 1979). It is a superlative index because it is a true index associated with a flexible functional form that is a quadratic mean of order two in this case (Hill 1993). The Sato-Vartia index is an exact index for more limited function that has two commodities with a constant elasticity-of-substitution (CES) function (Lau 1979). It is not necessarily exact for n commodities with a CES function and it is not a superlative index since the CES function is not a flexible functional form. Therefore, the Sato-Vartia index is not as well-known as the Torqvist approximation to the Divisia index.

Both the Torqvist approximation to the Divisia index and Fisher's index are symmetric indexes which attach equal weight or importance to the two situations being compared (Hill 1993). Basically, the symmetric index is preferred to either the Laspeyres or Passche indexes. Hill (1993) also noted that the precise choice among symmetric indexes is of secondary importance because all of them are likely to approximate each other and the underlying theoretic index fairly closely.

The above brief descriptions are intended as an introduction to the theory of index numbers, which will be applied to the decomposition method in this study. The price indexes used by the BLS are based heavily on the concept of the Laspeyres index. However, economists recently have been searching to improve the index. Certainly, the index for pharmaceuticals is of interest because pharmaceuticals have unique characteristics, which were mentioned before, such as rapid technological change. The following section will discuss the existing studies related to price indexes for pharmaceuticals.

Indexes for Pharmaceuticals

In the U.S., the Bureau of Labor Statistics (BLS) has published 2 types of price indexes, which are the Producer Price Index (PPI) and the Consumer Price Index (CPI). The PPI is compiled from average changes in selling prices received by domestic producers for their output (BLS 1997). The PPI is intended to emphasize industrial prices, which are based on prices received by producers from whomever makes the first purchase. The PPI is calculated according to a modified Laspeyres formula. The PPI is used for a lot of purposes by government, business, labor, and other kinds of organizations. The BLS publishes an overall price index for pharmaceutical preparations which has the Standard Industrial Classification (SIC) number 2834, and for 50 prescription pharmaceutical product classes. The reliability and accuracy of PPIs are critical to understanding the substantial growth in health care expenditures, because they usually are used in deflating current dollar expenditures to obtain a measure of real output growth by an industry. PPI growth rates also are used to assess inflationary pressures and pricing behavior in the health care sectors. According to Berndt et al. (1996), although the PPI is an output price index for a specific industry, such as pharmaceuticals, it is also an input price index for wholesalers who sell to retail drug stores and chains, mail-order firms, hospitals, and managed care organizations.

The CPI is the average change in the prices paid by consumers for a fixed market basket of goods and services (BLS 1997). The CPI was originated during World War I. It is essential for computing cost-of-living adjustments in wages. The BLS identified and defined a fixed market basket from Consumer Expenditure Surveys. The item structure is usually updated every ten years. The CPI is calculated by a modified Laspeyres price index, which is a chaining process. The government uses trends in the CPI in formulating fiscal and monetary policies. Business executives, labor leaders and other private firms use the CPI in making economic decisions. BLS publishes CPI-drugs as a consumer price index for prescription drugs and medical supplies.

Even though the PPI and CPI have been used for a long time, economists have still been working on how to improve the PPI for pharmaceutical preparations and the CPI-drugs because pharmaceuticals are very unique and include rapid technological change. Several studies commented and offered improvement for the PPI for pharmaceutical preparations and CPI-drugs. Cleeton et al. (1992) examined how the CPI-drugs was constructed by the BLS and also compared the conceptually desirable attributes of a fully quality-adjusted prescription drug price index. How the CPI-drugs excluded new products, which had no previous prices, was criticized. The new products were not included in CPI-drugs at the time of their introduction. Therefore, the CPI-drugs might be biased upward, downward, or not at all, depending on whether the imputed change in the price of the new drug, adjusted for quality, would be smaller or larger than the weighted average change in drug prices used to compute the CPI-drugs. Also, the way it incorporated new drugs, CPI-drugs did not indicate changes in knowledge about the quality of existing drugs. CPI-drugs showed a non-constant quality price index of a changing set of drugs was rising relatively rapidly. It would be useful to measure the change over a period in a price index that held quality constant by adjusting the prices of drugs for the changes in quality they represent. The interpretations of CPI-drugs would be limited because the adjustment process was difficult. Another problem of the CPI-drugs was when new drugs substituted for a non-drug therapy, a price index for drugs would mislead the indicator of the cost of health care. It also should be noted that CPI-drugs measured the change in drug prices for only cash payment transactions at retail pharmacies; it did not include prescription drugs purchased by managed care plans, Medicaid, and other third parties on behalf of individuals.

Berndt et al. (1990) compared price indexes constructed from the universe of products from a large multi-product pharmaceutical manufacturer in the U.S., with price indexes constructed from the particular products of this firm sampled by the BLS. A main finding was that price indexes based on the BLS sample of this firm increased similar to the published PPIs for SIC 28341, but price indexes computed using the universe of products produced by the firm increased much more slowly. The way in which new products were incorporated into price index computations had a substantial empirical impact on the rate of growth of the price index. Berndt et al. (1990) concluded the BLS tended to undersample new products that experience less than average price increases and oversample medium-age products that undergo above average price increase. In this study of the U.S. pharmaceutical industry from 1984 through 1989, the share of new and relatively new goods was significant, and failing to incorporate new goods promptly into price index computations may have resulted in upward-biased growth rate.

Griliches and Cockburn (1993) and Fisher et al. (1995) examined the issue of new goods and price indexes for the case of generic and branded drugs. When generic drugs were treated as entirely distinct goods and linked to indexes with fixed weights, the standard price indexes failed to reflect the substantial welfare gains to those consumers who regard generic and branded versions of a drug as being perfect substitutes. Detailed data on wholesale prices of anti-infective drugs were obtained to discuss the treatment of heterogenous consumers in constructing aggregate price indexes, and then various alternatives to the official indexes were computed. The results showed both heterogeneity of tastes for brandedness, and also the empirically important phenomenon of diffusion of generic drugs into the market following patent expiration. For instance, the BLS approach provided an increase in the wholesale price index of cephalexin about 14 percent over the 45 months of observation. At the opposite extreme, presuming the branded and generic drugs were perfect substitutes, the price decreased 53 percent.

Berndt et al. (1996) mimicked the BLS procedure and proposed some procedures for tracking producer prices in general and antidepressant drugs in particular. The market for antidepressant drugs was selected because of its dynamic features. Eight of the 21 studied entities on the market in 1996 were entirely new, having been introduced to the market within the last decade, and an additional seven brands experienced new generic competition after their patents expired. Theories and evidences of alternative price indexes were discussed. Three ways of introducing a link between generics and their patented antecedents were considered. First, for an "FDA Average Price Procedure", generics and branded versions of the same chemical entities were treated as perfect substitutes, and the average price of the entity was a current-month weighted average of generic and branded versions. The overall price index grew less than half as fast as it did when there was no linking to generics. Second, Griliches-Cockburn using an adjusted "Paasche Diffusion" method (GCPD) showed average annual growth rates of price indexes declined to a third lower than they were in the unlinked indexes. Third, "New BLS Procedure with Fixed Split Generic-

Brand Weights" mimicked the new procedure adapted by the BLS in May 1996. The results generally gave an impact in between the FDA and GCPD procedures. These results showed that the old BLS policy of not linking prices of newly introduced generics to the prices of their branded predecessors caused a very substantial upward bias on the overall price index for the studied antidepressant drugs. However, all these effects depended on which products would lose their patent protection and how important they were. A hedonic price analysis was undertaken to capture and quantify the quality improvements of new drugs over time. The hedonic price approach instead applied quality attributes as regressors, in effect making parameters on the brand dummy variables functions of quality attributes. It was noted that price indexes linking in new products using the predicted price from hedonic regressions could grow at rates less than, the same as, or greater than those that entirely ignore that link and instead incorporated only the price changes after new product launch. The rates of growth depended on whether the price of the new drug at its launch time was above or below that predicted by the hedonic regressions, given the new product's quality characteristics.

Other than the CPI and PPI, some prescription drug price indexes were developed in order to improve tracking prices. Kucukarslan et al. (1993) summarized pharmaceutical pricing studies and included some interesting studies. For instance, in 1974, Cocks and Virts calculated an index that measured prices per unit for 10 therapeutic classes. Actual prices rather than published list prices were used because they argued that list prices did not reflect the discounting that occurs in the prescription drug market. In 1992, the PRIME Index was developed by the National Association of Chain Drug Stores (NACDS) and Stephen

Schondelmeyer, to track the change in manufacturers' prices for the mix of drugs sold through traditional community pharmacies. In 1993, Kolassa measured changes in prescription drug prices of 71 of the top 200 prescription drug products sold in retail pharmacies in 1992. The selected products were kept constant for the 1989 through 1992 study period. This sample was chosen to limit the evaluation to price changes rather than including the impact of new products. Kolassa's price change index was a simple arithmetic mean rather than the weighted mean used by the PRIME Index.

Decomposition Methods

This section is intended to review methods used for separating the effects from factors contributing to the expenditures. Not only the previous studies related to prescription drug expenditures, but also others which contained decomposition methods, will be discussed.

To my knowledge, no single study yet has offered any standard structure of decomposition methods for expenditures. Most of the existing studies basically proposed a method that fit into their own study nature, such as the database available or the study objectives. However, generally, the decomposition methods used are either an additive or mutiplicative approach.

Jacob (1997) derived a separation method for the growth in health care costs. Total cost was separated into two components, average cost per unit (called AC) and the number of units (called Q), then total cost is the product of AC and Q. The equation for the separating calculation presented the growth rate of cost in terms of the growth rates of the two components of cost (unit cost and unit), plus a residual term. Assuming that the product of two components from cost and unit changes, [Δ(AC)* Δ(Q)], was of relatively small magnitude, the residual term could thus be approximated by zero.

$$\Delta\text{Total cost} = \Delta(AC) + \Delta(Q) + [\Delta(AC) * \Delta(Q)]$$

The formula can also be modified to account for the contribution of separate factors to the overall growth of costs when three or more variables form a product. It was noted that this formula obtains approximations, not precise figures. In 2000, Altman et al. examined the effects of enrollee mix, treatment intensity, and cost in competing indemnity and HMO plans. An additive equation was used to decompose cost differences across plans into effects attributable to mix, intensity, and prices for a wide range of conditions. The analysis only contained the primary effects, but it omitted the second-, third-, and fourth-order covariance terms, which were composed of 11 interaction terms. The interaction terms were not well explained.

In Canada, Anderson et al. (1993) examined the relative importance of changes in prices of services, the number of individuals eligible for services, and the rate of use per capita in determining changes in utilization and expenditures using an additive approach. Changes in population size, population distribution, and utilization rates all were evaluated by considering their independent effects on expenditures that were calculated by changing one of these factors while holding the other two constant. The study also realized that each of these factors changed over the study period, and there were interactions among these factors that account for the balance of the difference in expenditures. The interaction or residual term accounted for almost 7 percent of overall expenditure change. Mamdani et al. (2000) used an additive approach to determine the driving factors of antidepressant drug costs in Ontario, but no interaction term or residual was mentioned.

Cromwell and Puskin (1989) offered the methods and data used to make a discretionary reduction in the update for productivity gains, taking into consideration the shift to outpatient care. A multiplicative decomposition method was used to separate the accommodation's direct expenses per hospital discharge. First, the accommodation's direct expenses per hospital discharge was written in terms of the direct cost per discharge from a specified accommodation (DC/D) weighted by the share of discharges from this unit in total discharges or the unit admit rate (Dj/D). The accommodation-specific discharge cost then was decomposed into four elements:1) an expense-to-salaries ratio (DC/SAL); 2) a direct salary expense per paid hour (SAL/HR); 3) hours per patient day (HR/PD); and 4) patient days in each unit per discharge from the unit (PD/Dj). In summary, the equation became:

$$(DC/D) = (DC/SAL)*(SAL/HR)*(HR/PD)*(PD/Dj)*(Dj/D)$$

A concern was noted for using this equation to decompose trends in cost per case. The concern was that where annual trends are large (e.g. greater than 10 percent) and positively correlated, the sum of the individual right hand-side increasing rates will be less than the total increasing rate in cost per case because of interactions, and vice versa if individual trends are negatively correlated.

In Sweden, Gerdtham et al. (1993 and 1998) used a mutliplicative model to examine prescription drug expenditures. The increase in drug expenditure was analysed by separating it into three components, which were relative price of drugs, quantity and a residual. These three factors were presented in a multiplicative equation. The index number was used to evaluate the relative price change, while the quantity was determined by defined daily doses. The residual, which was the largest magnitude, primarily contained the effect from switching to more expensive drugs.

Previous studies focusing on prescription drug expenditure changes primarily used the concept of multiplicative growth models. For the U.S. studies, Express Scripts (2000) noted very briefly that the total expenditure change was calculated by multiplying the percent change of each factor. Evidently, the multiplicative approach might have been applied. Suh et al. (1999) and Dubois et al. (2000) mentioned specifically that a multiplicative growth equation was used to separate the price and volume factors.

Application of Index Number Theory to Decomposition Method

The theory of index numbers has been applied not only to capture the dynamic of price and quantity, but also to help solve problems in other area. The decomposition of changes in industrial energy consumption has been one of those major areas (Ang and Choi 1997). The development of the decomposition methods is analogous to the index number in economics (Liu et al. 1992). The primary purpose of decomposition in energy studies is to estimate the relative contributions from changes in product mix and in energy intensity to changes in the energy indicator being decomposed. Hankinson et al. (1983) examined the changes in industrial structure and in the intensity of electricity use within major industries by using a simple arithmetical procedure. However, the method used was ambiguous. A few years later, Reitler et al. (1986) proposed a method to determine the same factors as Hankinson et al. (1983) in an unambiguous manner. The mathematical method of total differentials was used to decompose the factors. The result of the total difference in energy consumption was shown finally as an additive form of all factor changes. However, Park (1992) showed that the method used by Reitler et al. failed to introduce structural change explicitly. A residual term, which was composed of the interactions of each effect, then was separated from the effect of structural change in this study. In 1988, Boyd et al. introduced an index number to approach the decomposition of one of the factors studied in Hankinson et al. (1983) and Reitler et al. (1986), which was energy intensity. The Divisia index approach was used in the study. The Divisia index approach, a variable weight index, was claimed to be superior to the fixed base approach, such as Laspeyres index, because the Divisia index approach could better capture rapidly changed energy data. Also, the Divisia index approach satisfied several favorable index properties.

The most often used decomposition methods in industrial energy studies are Laspeyres index and Divisia index approaches (Ang and Choi 1997). For the Laspeyres index method, each main effect is extracted by measuring a change in energy consumption or aggregate energy intensity associated with a change in the corresponding variable from year 0 to year T. All other variables are held constant at their respective values in year 0. One or more interaction effects are included, depending on the number of the main effects. The interaction effect, which sometimes is called the residual term, does not have much economic meaning. Fundamentally, the Laspeyres index method was presented clearly by the additive approach of the decomposition in Ang and Choi (1997).

Generally, the Laspeyres index approach can be presented algebraically as follows. Let A be the aggregation of a variable A_i, which has each share as b_i. Algebraically, A can be presented as follows:

$$A = \Sigma\, b_i\, A_i \qquad (1)$$

Let D_{total} be the ratio of the aggregation of year T to that of base year 0

$$D_{total} = A_T/A_0 \qquad (2)$$

$$A_T = \Sigma_i b_{i,T} A_{i,0} + \Sigma_i b_{i,0} A_{i,T} + \Sigma_i (b_{i,T} - b_{i,0})(A_{i,T} - A_{i,0}) - \Sigma_i b_{i,0} A_{i,0} \qquad (3)$$

After dividing by A_0, (3) becomes

$$D_{total} = D_b + D_A + D_{interaction} - 1 \qquad (4)$$

where

$$D_b = (\Sigma_i b_{i,T} A_{i,0})/A_0 \qquad (5)$$

$$D_A = (\Sigma_i b_{i,0} A_{i,T})/A_0 \qquad (6)$$

$$D_{interaction} = (\Sigma_i (b_{i,T} - b_{i,0})(A_{i,T} - A_{i,0}))/A_0 \qquad (7)$$

Therefore, D_b, D_A, and $D_{interaction}$ represent the estimated effects of b and A given by the decomposition method.

The conventional Divisia index, Tornqvist discrete approximation to the Divisia index, was applied to industrial energy decompositions in late 1980s (Liu et al. 1992). It uses the weighted average of logarithm changes of the relevant variables, which leads to a residual term because of the approximation of the theoretical continuous Divisia index (Ang and Choi 1997). The decomposition using the Divisia index method can be expressed in the multiplicative form.

The Divisia index approach can be presented algebraically. Assuming all variables in (1) are continuous and given as functions of time t, the growth rate of A can be presented as

$$dln(A)/dt = \Sigma\, w_i[dln(b_i)/dt + dln(A_i)/dt] \qquad (8)$$

where $w_i = (b_i A_i)/A$ and is also function of t, which will be defined below. Integrating equation (8) with respect to t over the time interval 0 to T and rearranging the terms gives

$$D_{total} = D_b * D_A \qquad (9)$$

where

$$D_b = \exp[\Sigma_i(w_{i,T} + w_{i,0})/2\ \ln(b_{i,T}/\ b_{i,0})] \qquad (10)$$

$$D_A = \exp[\Sigma_i(w_{i,T} + w_{i,0})/2\ \ln(A_{i,T}/\ A_{i,0})] \qquad (11)$$

which actually is the Tornqvist discrete approximation to the Divisia index approach.

Ang and Lee (1994) and Ang (1994) examined some methodological and application issues of the decomposition of industrial energy consumption. A general framework of the decomposition was offered. The framework was composed of additive and multiplicative decompositions. Several methods based on the theory of Laspeyres and Divisia indexes were compared and discussed. The studies concluded that there did not exist a certain best way of decomposition. The analysts suggested continued choosing any method from a specific set of criteria. One of the highly suggested criteria was that the preferred method should give a residual term close to ideal value, which was 0 for the additive decomposition and 1 for the multiplicative decomposition. However, all methods reviewed contained more or less residuals.

Perfect Decomposition (Refined Divisia Index Method)

Even though the Divisia index approach is more preferable than the Laspeyres index for several reasons mentioned above, using the conventional Divisia index method in the decomposition carries more or less the residual term, which was not shown in the equation (9). Sato (1976) discovered the log-change index number and it was used particularly as an approximation to the theoretically desirable Divisia index, which actually is Sato-Vartia index number formula. Ang and Choi (1997) applied the ideal-log change index formula developed by Sato in 1976 to get rid of the residual. Instead of using the arithmetic mean weight formula, the logarithmic mean weight was used. The formulae become

$$D_b = \exp[\Sigma w_i^* \ln(b_{i,T}/ b_{i,0})] \quad (12)$$

$$D_A = \exp[\Sigma w_i^* \ln(A_{i,T}/ A_{i,0})] \quad (13)$$

where

$$w_i^* = \{[(w_{i,T} - w_{i,0})/\ln(w_{i,T}/ w_{i,0})]/ \Sigma[(w_{i,T} - w_{i,0})/\ln(w_{i,T}/ w_{i,0})]\} \quad (14)$$

Applying (12) and (13) to the decomposition leaves no residual, which was proven in Ang et al. (1997). The results (12) and (13) are called refined Divisia indexes, which give perfect decomposition. The refined Divisia index method always can be applied to more than two-factor equations.

After the refined Divisia index was introduced to decompose factors affecting energy consumption or intensity in 1997, its application was included in three other energy studies

(Ang et al. 1998, Ang and Zhang 1999, and Zhang and Ang 2001). The refined Divisia index approach was proved to be superior to conventional decomposition methods including Laspeyres and Tornqvist discrete approximations to the Divisia indexes, which leave unexplained residuals from the decomposition. These residuals may be relatively large, depending on variation in factors. The refined Divisia index also was proved to be more robust, and provided more complete results regardless of the data pattern.

Ang (1994) concluded from an empirical study that there were small differences between using an additive and multiplicative approach. However, further analysis is needed. Generally, the criteria of method selection are whether the chosen method meets the objective of the study, ease of use, and whether the method gives no residual. Also, Boyd et al. (1988) suggested that a way to overcome the selection problem is to postulate a functional relationship between the factors being studied. However, none was proven in the energy study. It is noteworthy that the issues of exact or superlative index numbers have never been discussed in energy studies.

None of studies in the health care field yet have applied the concept of perfect decomposition to isolate the factors contributing to the expenditures. In fact, none of the decomposition methods using economic theory of index numbers applied to this field have existed before. The Laspeyres index, Torqvist approximation to the Divisia index, and refined Divisia index were used in this study because no single perfect index or decomposition approach existed. The three indexes allowed us to examine both additive and multiplicative approaches, and various possible functional forms of factors. In other words, all three indexes used in this study provided a more complete picture of the factors affecting prescription drug expenditure changes than a single index or decomposition approach study.

Research Significance

In 1992, Newhouse mentioned that there was no good empirical basis for decomposing the drug expenditure increase into increases in price and increases in quantity. However the pharmaceutical market has been changing rapidly and is increasing of interest. Also, prescription drug expenditures recently have become an important political issue that has been discussed very heavily since the government has been proposing Medicare prescription drug coverage. A concern about this new policy is that it will escalate the prescription drug expenditures more. The issue of factors affecting the prescription drug expenditures thus has been focused recently. For instance, in 2000, the U.S. President urgently requested the Department of Health and Human Service to study prescription drug coverage, spending, utilization and prices in order to identify the problems that may happen after launching a Medicare prescription drug coverage policy. Better projections or studies always help improve future policy. The Health Insurance Association of America (1999) found that predicting future trends of spending for prescription drugs was difficult. Others have been challenged when attempting to predict changes also. For instance, in early 1999 the HCFA estimated that prescription drug expenditures would be $171 billion or 9.2 percent of the total personal health care expenditures in 2007. After six months, HCFA learned more, and then changed their projection. By mid 1999, the HCFA predicted that prescription drug expenditures should be $223 billion or 12.4 percent of the total, instead. This reflects that a greater understanding allows more precise prediction.

Within last 2 years, several studies were conducted. Evidently, the factors affecting prescription drug expenditures are more than price and quantity effects. The effect of technological change, which is reflected by product mix effects, should be included. The previous studies tried to identify the effects of all factors. However, only some of the studies reported the individual effect of each factor separated from others, but most of studies included two or more effects into one factor. Also, since the existing studies were designed to serve different audiences or organizations, various definitions, concepts and methods were applied to capture the factors affecting the prescription drug expenditures. Therefore, the mixed results of the relative importance of all factors were found. Moreover, none of the previous studies showed how they calculated the relative magnitudes of the effects, which did not allow the readers to repeat or use the methods for the other settings. This created ambiguous results and made readers or policy makers more skeptical.

This study defined each factor affecting the prescription drug expenditures. Various decomposition methods were applied to break down all factors. The decomposition procedure was based on several economic index numbers, which have been widely used in various businesses and gives easily interpreted results. The working mathematical formulas of the indexes were shown and used to calculate the relative magnitudes of the factors.

CHAPTER 3

METHODS

The first section of this chapter will define variables used throughout the study. The second section describes data collection methods and then last section explains data analysis

Definition of Variables

Figure 3.1 shows the logical flow of the study approach. The study was mainly divided into two steps. The first step was a descriptive analysis and the second step factoring the relative magnitude of the effects of price change, utilization, prescription size, and product mix on prescription drug expenditure changes.

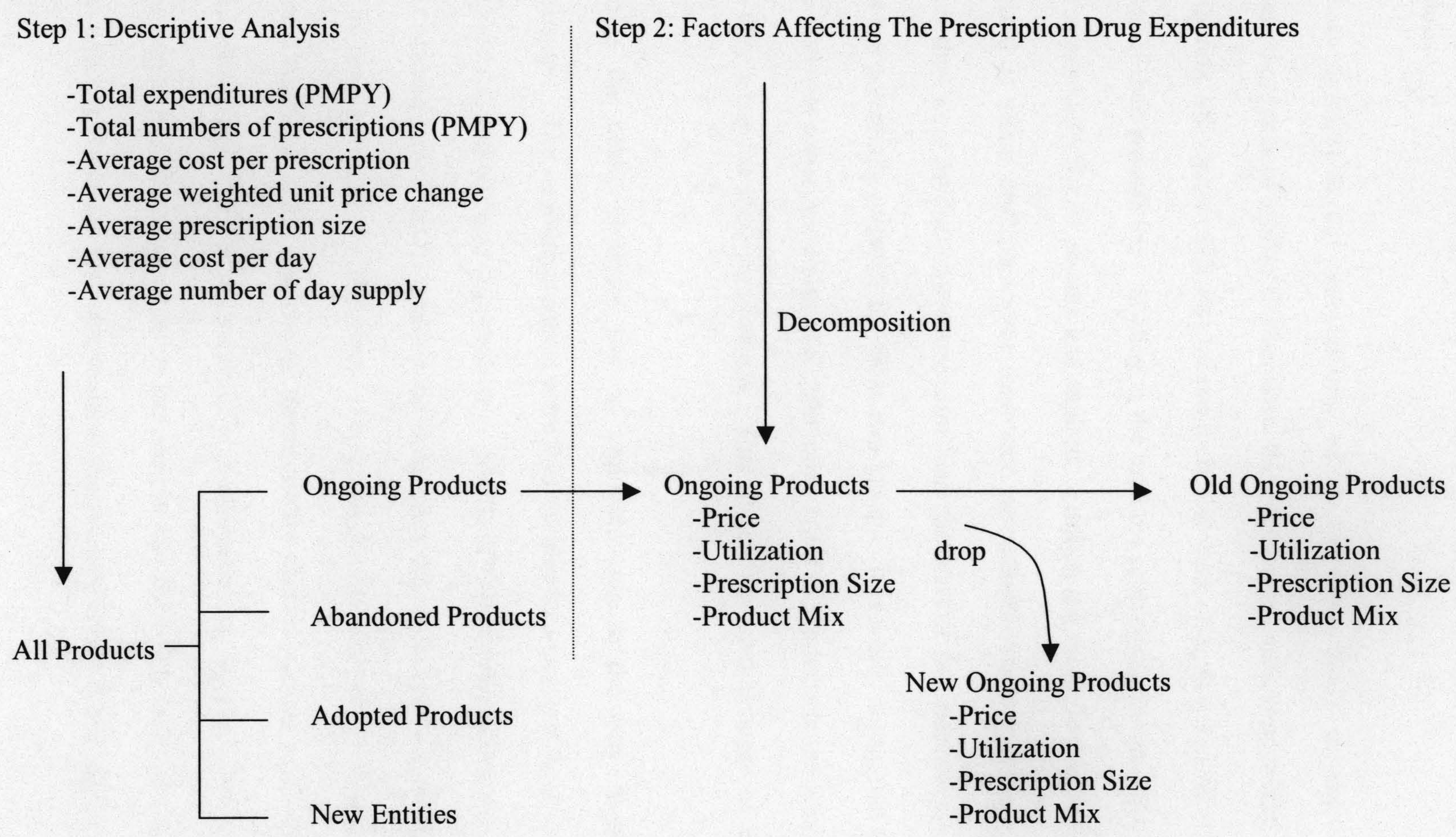
In the first step, all descriptive analyses were performed for overall products and also partitioned into types of drug products. Drug products were categorized in several ways, which depended upon what kind of information was needed. To facilitate the index number calculation, the drug products were categorized depending upon whether claims appeared in both years of data being compared.

1. Ongoing product: product claims were present in both years, which were consecutive years.

2. Abandoned product: any product, which was used in the first year, but it was not available or used in the second year of the period.

3. Adopted product: any product that was available in market, but it had just been used in the second year, not in the first year of the period.

Figure 3.1 The Logical Flow of Data Analysis



4. New entity: any product, which has just been launched to the market during the period. It was then categorized into the three groups above in the following periods.

By these definitions, the new entities, which are more likely expensive, were separated from other types of products. Therefore, this interesting group was tracked clearly. Then those ongoing, abandoned, and adopted products also were categorized as either single-source products if their patents were existing at the time the prescriptions were dispensed or multiple-source products if their patents had expired. Further, the multiple-source products were categorized as either multiple-source innovator, or multiple-source generic products, due to whether they were products from innovator manufacturers or not, because prices and price changes are potentially different for those two groups. It is worth noting that the new entities of the previous period were separated from other types of products in the later period, even though they were the ongoing products. This clearly revealed changes of the new entities

Basically, the newer products play an important role in the prescription drug expenditure changes. The ongoing products were thus divided into two groups which were new ongoing products and old ongoing products. Merlis (2000) concluded that the relative importance of old and new drugs in prescription drug expenditure changes depended on the cutoff point of time between old and new. According to Pharmaceutical Research and Manufacturers of America (2001), the average patent life for pharmaceuticals after U.S. Food and Drug Administration (FDA) approval is approximately 10 years. We therefore considered the ongoing products, which were launched within five years before the analyzed period, as new ongoing products. Two subgroups of the ongoing products were defined.

1. New ongoing products: any ongoing products that were launched within five years before the study period.

2. Old ongoing products: other ongoing products that are not new ongoing products.

In the second step, since the study's objective was to estimate the relative magnitude of inflation, utilization, prescription size, and product mix on prescription drug expenditure changes, all of these factors should be defined. However, the definitions of product types in the first step still were applied. Also, since the theory of index numbers was used to decompose all factors, only ongoing products were analyzed in this step because the availability of price and quantity for both years in the study periods was needed for calculating the indexes. The rate of change of prescription drug expenditures were reported in terms of the change of cost of prescription drug per member per year (PMPY). Even though a constant number of enrollees was used, reporting by using cost per member per year was consistent and, thus, comparable with the previous studies, such as Merck-Medco (2000) and Express Scripts (2001), and easily interpreted. The cost of prescription drug PMPY was composed of two major components, which were cost per prescription and number of prescriptions PMPY. The change of number of prescriptions PMPY was defined as the effect of utilization change, while the cost per prescription was broken down into three components, which were the effects of inflation, prescription size and product mix. The effect of inflation was the effect of AWP price change per unit for each prescription drug, the effect of prescription size was the change in number of units per prescription, and the effect of product mix was the change of distribution between more or less expensive prescription drugs utilized.

The product mix effect also was categorized in terms of dosage strength, and therapeutic agents mix and/or drug class mix used in the database as following.

1. Strength mix: an impact on product mix effects from different strengths used, in cases where products had more than one strength.

2. Therapeutic mix: an impact on product mix effects from shifting in utilization to more or less expensive therapeutic agents or drug classes in drug groups

Data Collection

Previous studies showed the degree to which various factors affected prescription drug expenditures across therapeutic drug categories (Barents Group 1999, Dubois et al. 2000, Merck-Medco 2000, and Express Scripts 2001). DiMasi (2000) suggested that it was necessary to study prices at the specific therapeutic category level or even at the individual drug level to understand drug pricing patterns. The main goal of this study was to develop a tool that captured the effects of inflation, utilization, prescription size, and product mix on drug expenditure changes. It would be very laborious, if all therapeutic drug categories were analyzed. Therefore, the study only intended to empirically show how the developed tool can be used in an example therapeutic drug category, anti-diabetic drugs.

Anti-diabetic drugs were chosen because they have been high use and a high percentage of drug expenditures for several years (Riley et al. 1998 and 1999, Barents Group 1999, and Friedman and Kulp 2000). Merck-Medco (2000) reported that anti-diabetic drugs are one of five drug categories that will account for more than 75 percent of future drug trends. Mullins et al. (2000) reported that approximately 40 drugs for endocrine, nutritional, metabolic and immunity treatment, including anti-diabetic drugs, were on a list of expected drug patent approvals between the years 2000 and 2004. Anti-diabetic drugs also are very specific to particular symptoms, which make them a good representative for a disease specific therapeutic category. Anti-diabetic drugs also are a long term drug treatment. Therefore, continuous anti-diabetic drug users were more likely stable and easily obtained.

It is predicted that more aggressive diagnosis and management of diabetes will induce higher utilization of oral hypoglycemic agents (Merck-Medco 2000). Several new drugs for diabetes are in the pipeline, including new dosage forms of insulin and two "aldose reductase inhibitors", plus the patent for Glucophage® expires in year 2001. Even though the expenditures for anti-diabetic drugs have been much lower than for other therapeutic drug groups, growth in the share of spending represented by new drugs among anti-diabetic drugs has been high (Barents Group 1999).

The American Diabetes Association's criteria for diagnosis of diabetes was changed due to a revision in 1997. Fasting blood glucose levels of 126 mg/dL (instead of 140 mg/dL) or higher and its confirmed result on a subsequent day were used to diagnose diabetes (American Diabetes Association 2001). This guideline was consistent with the suggestion from the Diabetes Control and Complications Trial (DCCT) that tight management of blood sugar reduced the risk of diabetic complications. The American Diabetes Association's guideline and DCCT suggestion encouraged more-intensive medication regimens. To increase control of the disease, patients may have received combination medications or higher doses. It was recommended that switching to another pill was usually less effective than adding another type of diabetes drug. These diagnosis and treatment guideline changes supported the increase in diabetes drug expenditures.

There also seems to be sufficient product mix among anti-diabetic drugs. It is a drug group that includes agents with several drug actions that are combined or substituted for each other routinely. Among anti-diabetic drugs, there exist dramatically different prices per unit, even though they have the same basic mechanism of action, or sometimes the same generic name. It also had some interesting characteristics during the previous period, such as a new entity launched to the market, new strength and new dosage forms of existing products, and some agents became obsolete or at least were not used. Therefore, the anti-diabetic drug group was a good example for this study.

The sources of data were prescription claim records and enrollment data from the Unity Health Plans (UHP), a health maintenance organization in Wisconsin. Unity Health Plans began providing community-based managed care products and services in 1994. It serves more than 80,000 members in half of all Wisconsin counties. It has an array of health care plans, including HMO, Point-of-Service, and Self-Funded plans. Each member is one of three provider networks, the Unity Provider Network, the UW Health Provider Network and the Community Provider Network. The Unity Provider Network allows members to choose a Primary Care Physician (PCP) from all participating PCPs. The UW Health Provider Network has a relationship with the University of Wisconsin-Madison Medical Center and primarily relies on affiliated physicians to provide care to members. Members of the

Community Provider Network can choose physicians and specialists throughout southwestern Wisconsin, including the University of Wisconsin-Madison Medical Center.

Claims data were chosen because they were not subject to the recall problems that usually are found with self-reported data (Momin et al. 2000). Also, they provided accurate information on prescription drugs dispensed for reimbursement purposes. Generally, all prescription drugs were covered in the formulary of the health plans, except smoking cessation medications, cosmetic medications, infertility, and obesity agents. However, exceptions sometimes were made. Non-formulary products were covered when formulary products had failed to obtain the desired results.

Unity reimbursement to pharmacies from 1996 to 1997 was 90 percent of Average Wholesale Price (AWP) plus $2.50 dispensing fee or maximum allowable cost (MAC) plus $3.25 dispensing fee for the multiple-source generic drugs chosen to apply their MAC policy to. Patients could get a brand name product, but if a generic version was available, they had to pay the difference between MAC or generic name product cost and brand name product cost. However, the reimbursement policy has been changed since 1998. It highly depended on particular drug products. Clarifying information on payment variation across products was not available.

The prescription drug claims of anti-diabetic drugs were obtained from Unity Health Plans via the pharmacy service director by electronic mail and downloaded to a personal computer. The data were originally formatted with Microsoft Excel. The data were composed of seven separated files, including five prescription claims files, an enrollees' identification file, and a summary of numbers of enrollees. The prescription claims record data were a separated five-year retrospective database from January, 1996 to December, 2000. All seven files provided the information from only continuous enrollees.

For the five prescription claims files, data elements included member identification numbers, gender, date of birth, fill date, National Drug Code (NDC) number, Generic Product Identifier (GPI) code, drug name and strength, pharmacy plan, quantity, number of days supply, ingredient cost, copayment, dispensing fee, pharmacy reimbursement requested and amount paid. The enrollees' identification numbers were de-identified in the data to protect confidentiality. The enrollees' identification file included identification number, birth date, and gender for all continuous enrollees, while the summary of numbers of enrollees accounted the numbers of continuous enrollees across those five years.

The first two digits of the GPI code, "27", were used to confirm anti-diabetic drug claims. Then the prescription claims files were converted to Microsoft Access for data processing purposes. Originally, there were 5,322 records in 1996, 6,401 records in 1997, 7,745 records in 1998, 9,276 records in 1999, and 10,657 records in 2000. There were 43 records with zero value in quantity, number of days supply, ingredient cost, copayment, dispensing fee or pharmacy reimbursement requested and amount paid in 1996 claims file, while there were 102, 464, 569, and 749 of those zero values in 1997, 1998, 1999, and 2000 files, respectively. There also were three and one reversed claims, which should not be included in prescription expenditure data, in 1996 and 2000, respectively. These non-usable records were deleted from the data files. After removing these unusable records, there were 5,276 records in 1996, 6,299 records in 1997, 7,281 records in 1998, 8,707 records in 1999, and 9,907 records in 2000 for all continuous enrollees.

Data Analysis

The claims data from all continuous enrollees were descriptively analyzed and summarized. However, claims data from continuous anti-diabetic drugs users, among those continuously enrolled in UHP (members enrolled for the five-year study period and had used anti-diabetic drugs since 1996), served as a major analysis group throughout the entire study. In so doing, the factors affecting the prescription drug expenditure changes were the contribution of how products have been used, such as the growth of the prescription drugs including substitution from older products (Thomas 2000), not from the enrollee mix. Even though the analyzed enrollees were fixed, their treatment patterns might be changed across times due to practice guidelines. Enrollment data were incorporated in calculations whenever per member analyses were desired.

Generally, the overall expenditures for a managed care organization are the aggregation across claims paid of ingredient costs plus dispensing fee less copayment. A primary part of the expenditures is total ingredient costs, thus this study used total ingredient costs as the analysis of expenditures.

Since the study planned to analyze cost per prescription and price effects, one of the key data elements was the price per unit. A representative unit price of each product NDC number in each year needed to be determined. Ngorsuraches (1999) determined regular and consistent changes occurred in the modes of the unit prices in claims data from the same HMO that was used in this study. After converting costs per unit to AWPs, the prices in the claims data also were found to be consistent with a price reference, the Red Book. Therefore, this study used the AWP from the Red Book as a unit price reference for each

NDC number. The ingredient cost analyzed were simulated ingredient cost since AWP was used instead of the HMO's reimbursed amount for ingredient cost (i.e. 90 percent of AWP).

It also was clear in Ngorsuraches (1999) that some multiple-source generic products were drugs primarily dictated by Maximum Allowable Cost (MAC) prices. Therefore, the AWPs from the Red Book were not appropriate unit prices for MAC products. The MAC drug list from the UHP was not available for all years in the study. Since the UHP is an HMO serving residents in the state of Wisconsin, the Wisconsin Medicaid MAC list from Wisconsin Medicaid Handbook (2001) was then used to identify and generate unit prices for MAC products. Since the MAC policy dictated product prices, and did not follow actual market prices, the policy effects needed to be removed to reflect the real effect of price changes on ingredient costs. To remove effects of MAC policy changes on the ingredient costs, all unit prices of the MAC products were replaced by their unit prices for 2001, which were available publicly from the Wisconsin Medicaid MAC list at the data analysis time, August 2001. It is worth noting that even though the "simulated" ingredient costs obtained might not be exactly those that UHP experienced, the effect from policy was eliminated and the inflation effect of other product groups stayed the same.

A working file of aggregated data was created for analysis convenience. Total quantities and numbers of prescriptions used in each year were tallied and summed for each NDC number. Prescription size or units per prescription was calculated. Then the unit prices were matched to those NDC numbers. The aggregated data working file was then composed of columns of 187 NDC numbers, drug names, quantity, prescription size and unit prices, and numbers of prescriptions for the five study years.

There are several ways to present the ingredient cost changes. Even though the goal of this study was to estimate the relative magnitude of effects of inflation, prescription size, utilization and product mix on the prescription drug ingredient costs, general descriptive information of the ingredient costs also was included to provide a broad picture. Therefore, the analyses were composed of two major steps. In the first step, general descriptive analyses were performed, while decomposition of factors affecting prescription drug ingredient cost changes was done in the second step.

The First Step: Descriptive Analysis

The first step was to determine the ingredient cost information from both all diabetes patients, who continuously enrolled in the UHP and only continuous anti-diabetic drug users who were continuous enrollees. This analysis provided general descriptive information of the data from both enrollee groups. To do so, quantities used in each year of each product were counted. They were multiplied by their AWP unit prices to get dollar amount spent on each product, then they were summed across products. A count was made of total number of prescriptions. Numbers of all diabetes patients, who continuously enrolled in the UHP were counted. Numbers of members who continuously used anti-diabetic drugs and continuously enrolled in the UHP also were counted. The number of prescriptions per member per year and total ingredient costs per member per year was calculated by dividing total number of prescription and total ingredient costs by number of counted enrollees, respectively. The amounts of change were computed for each element as the difference between two consecutive years, then converted to the percentage based on the first year of those consecutive years. To remove the enrollee mix effect that might interfere with other study effects, only anti-diabetic drug users who continuously enrolled in the health plan were analyzed further.

Since defined subgroups, including single-source, multiple-source innovator, and multiple-source generic groups, differently contributed to total drug ingredient costs, drug ingredient costs across all defined subgroups were calculated. Numbers of NDCs and numbers of drug entities that were different generic names with different strengths and forms were counted. In order to examine proportionately how different groups of products contributed to total ingredient costs, costs of ongoing products, adopted products, abandoned products, and new entities were calculated as the percentage of total amount of ingredient costs for each year. This was done with all subgroups of drug products too. It also was done on a per number of enrollees basis.

Then the changes in ingredient costs between the years were calculated as a percent of the total incremental change during the study periods. To determine the ongoing product cost change, the ingredient costs of the ongoing products in the first year of the period were subtracted from their costs in the second year of the same period, and calculated as the percentage of total amount of incremental change for the period. This was defined as the ongoing product cost change because these changes were the result from redistribution of quantities used within the ongoing product group.

The adopted and abandoned product cost change was computed as the difference between the total ingredient cost of the adopted products from the second year of a period and the total ingredient cost of the abandoned products from the first years of the same period. The total amount of the ingredient costs of abandoned products were subtracted from the total amount of the ingredient costs of the adopted products to identify product cost change, then was calculated as the percentage of total dollar amount of the incremental changes of each period. This also was done with those subgroups, single-source and multiple-source products. The new entity cost change was determined by the total ingredient costs of new entities added in a period. The total amount of ingredient costs of new entities was calculated as the percentage of total dollar amount of the increment for that period.

As a way to examine factors affecting the total ingredient cost changes, average drug ingredient cost per prescription, average unit price, and average prescription size were calculated. The average unit prices were weighted by their quantities used. This analysis determined how changes in price and prescription size affected the changing ingredient costs.

It became clear as analyses progressed that the average weighted unit prices were not the same unit across different dosage forms since both liquid and solid forms were available for anti-diabetic drugs. Some products had their unit price as per milliliter, while others had unit price as per tablet (or capsule). Therefore, average cost per day, which was weighted by numbers of day supply, was calculated across all types of products. Also, average number of days supply per prescription was calculated. This analysis provided more comparable results across product types since they were the same cost per day basis.

Numbers of NDC numbers of each categorization analyzed were counted to preliminarily screen the signal of product mix. There were several alternatives for examining the mix effect of products on the ingredient costs. Some products had more than one strength, and their unit prices were different. Certainly, using different strengths of a given product in each period was another kind of product mix that could be a factor in changing ingredient cost. To examine strength mix, numbers of prescriptions of products, which have more than one strength were counted. The proportions of total prescriptions for each drug that were attributed to different strength dosage forms of that drug were computed. Their costs per prescription also were calculated in order to compare across all strengths. The strength mix also was identified by multiplying the number of prescriptions and the milligram strength of each dosage form, summing the result, and then dividing by total number of prescriptions. This result gave average milligram strength per year for each drug.

The anti-diabetic drugs also can be divided into therapeutic subcategories. Each group had their own characteristics. Some of them have been used for a long time, some of them have just been launched into the market, some of them have been slightly used, and some of them have been heavily used. Certainly, their prices were different, and this caused some mix effects. Thus, therapeutic mix was examined in order to capture the distribution of numbers of prescriptions across therapeutic subcategories. Numbers of prescriptions for products, which had the same first six-digits of GPI were counted. They were computed as the percentage of the numbers of prescriptions of each year. Their costs per prescription also were calculated for the same reason as the strength mix's.

The Second Step: Decomposition of Factors Affecting Prescription Drug Ingredient Cost Changes

The second step of the data analysis was designed to examine the factors affecting prescription drug ingredient cost changes from the ongoing products. Then the effects of the abandoned products, adopted products, and new entities were included to capture overall product ingredient cost changes.

The theory of index numbers was applied to decompose the factors affecting the prescription drug ingredient cost changes from only the ongoing products because price and quantity information from two consecutive years was needed for index calculations. The changes of the prescription ingredient costs between the two-year period were determined by the changes of average cost of prescriptions PMPY. As defined above, the changes of average cost of prescription PMPY were composed of two major components, which are average cost per prescription and number of prescriptions PMPY. The change of number of prescriptions PMPY was defined as the effect of utilization change, while the cost per prescription was broken down into three components, which were effects of inflation, prescription size and product mix.

Since there was no reported standard decomposition method, and the study was intended to methodologically examine the effects of inflation, prescription size, utilization and product mix on the prescription drug ingredient cost changes, both additive and multiplicative methods were explored. As stated in the literature reviewed, there are many index methods for either additive or multiplicative decompositions. Only three index methods, the Laspeyres, Tornqvist discrete approximation to the Divisia index and refined Divisia index methods, were selected based on several reasons.

First, the Laspeyres index method provided additive decomposition, while the other two Divisia index methods exemplified multiplicative decompositions. Therefore this allowed both additive and multiplicative methods to be included in this study. Second, the Laspeyres and Tornqvist discrete approximation to the Divisia index methods are very well known in economic index studies. The Laspeyres index is one of the most common economic indexes. The BLS has been using the Laspeyres index as a basic concept to compute CPIs, which are widely used in various industries. The Tornqvist discrete approximation to the Divisia index is an exact index number when the function to be indexed is a translog function (Diewert 1978, Lau 1979, and Hill 1993). It is called a superlative index number, which is a true index number associated with a flexible functional form. It is therefore recommended by the CPI Commission to be used to calculate price indexes (Berndt et al. 1997 and Triplett 1999). Third, the Laspeyres index and Divisia index approaches were the most often used decomposition methods in industrial energy studies, which were the applications that this study was based on (Ang and Choi 1997).

Fourth, based on the energy studies, one of the highly suggested criteria was that the preferred decomposition method should give a residual term close to ideal value, which was zero for the additive decomposition or one for the multiplicative decomposition. Both Laspeyres and the Tornqvist approximation to the Divisia index methods contained more or less residuals. For instance, Laspeyres index method included at least four interaction terms in this study because there were three main factors in the cost per prescription drug ingredient cost. Even though the interaction terms in the additive approach usually were claimed to be not significant, they can alter the results from main factors, if the annual trend is high, e.g. more than 10 percent (Cromwell and Puskin 1989). The residuals or the interaction terms were not easily interpreted and basically were left without explanation. The refined Divisia index method, which provided multiplicative decomposition without residuals, and was proved to be more robust regardless of any data pattern, was then included into this study.

Algebraically, the decomposition can be presented as follows:

Let Cost PMPY = Average cost of prescription drug per member per year

Cost PRx = Average cost per prescription

U = Utilization (number of prescriptions per member per year)

P_i = Unit price of product i

S_i = Prescription size (unit per prescription) of product i

M_i = Product mix (fraction or share in the market) of product i

Therefore,

$$\text{Cost PMPY} = (U)*(\text{Cost PRx})$$

The Cost PRx was written as an aggregate form:

$$\text{Cost PRx} = \Sigma P_i S_i M_i$$

Then

$$D_{\text{cost PMPY}} = \text{Cost PMPY}_T / \text{ Cost PMPY}_0$$

$$D_{\text{cost PRx}} = \text{Cost PRx}_T / \text{ Cost PRx}_0$$

where 0 was the beginning year and T was the second year of the study period, and $D_{cost\ PMPY}$ and $D_{cost\ PRx}$ were the ratio of cost per member per year and cost per prescription, respectively, between year T and 0.

From the Laspeyres index method, the additive decomposition was presented as

$$D_{cost\ PMPY} = D_U + D_P + D_S + D_M + D_{residual} - 3$$

where $D_U = U_T/U_0$

$D_P = (\Sigma P_{i,T}S_{i,0}M_{i,0})/ (\Sigma P_{i,0}S_{i,0}M_{i,0})$

$D_S = (\Sigma P_{i,0}S_{i,T}M_{i,0})/ (\Sigma P_{i,0}S_{i,0}M_{i,0})$

$D_M = (\Sigma P_{i,0}S_{i,0}M_{i,T})/ (\Sigma P_{i,0}S_{i,0}M_{i,0})$

D_U, D_P, D_S, D_M and $D_{residual}$ were the relative effects of utilization, price, prescription size, product mix, and residuals respectively.

From the Tornqvist discrete approximation to the Divisia index method, the multiplicative decomposition was expressed as

$$D_{cost\ PMPY} = D_U*D_{cost\ PRx}*Dresidual = D_U*D_P*D_S*D_M*D_{residual}$$

where $D_U = U_T/U_0$

$D_P = \exp[\Sigma (w_{i,0} + w_{i,T})/2 \ln(P_{i,T}/ P_{i,0})]$

$D_S = \exp[\Sigma(w_{i,0} + w_{i,T})/2 \ln(S_{i,T}/ S_{i,0})]$

$D_M = \exp[\Sigma(w_{i,0} + w_{i,T})/2 \ln(M_{i,T}/ M_{i,0})]$

where $w_{i,0} = (P_iS_iM_i)/$ Cost PRx, at year 0

$w_{i,T} = (P_iS_iM_i)/$ Cost PRx, at year T

From the refined Divisia index method, the decomposition was presented as

$$D_{\text{cost PMPY}} = D_U * D_{\text{cost PRx}} * D_{\text{residual}} = D_U * D_P * D_S * D_M \; (D_{\text{residual}} = 1)$$

where $$D_P = \exp[\Sigma w_i^* \ln(P_{i,T} / P_{i,0})]$$

$$D_S = \exp[\Sigma w_i^* \ln(S_{i,T} / S_{i,0})]$$

$$D_M = \exp[\Sigma w_i^* \ln(M_{i,T} / M_{i,0})]$$

where $$w_i^* = \{[(w_{i,T} - w_{i,0})/\ln(w_{i,T}/ w_{i,0})]/ \Sigma[(w_{i,T} - w_{i,0})/\ln(w_{i,T}/ w_{i,0})]\}.$$

The decomposition methods were applied to overall ongoing products. The results provided the relative magnitudes of inflation, utilization, prescription size, and product mix effects. This reflected the effects from overall ongoing products on the total ingredient cost PMPY change.

Even though new ongoing products were not products launched during the analyzed period (defined as the new entities), the effects from the new ongoing products were expected to be important because of their diffusion period in the early years after being launched. To capture the activity of the new ongoing products, they were removed from the list of the overall ongoing products and decomposition calculations were repeated, yielding the effects from only old ongoing products. The differences between the effects of the overall ongoing products and old ongoing products were calculated to reflect the effects from new ongoing products. Only the Laspeyres index decomposition was used for calculating the effects from new ongoing products because the Laspeyres index was an additive approach and it allowed subtractions between the indexes from old and new ongoing products.

Since the price and quantity information of the abandoned products, adopted products, and new entities was not available for both first and second years in each period, the index approach was not applicable to capture overall ingredient cost changes. However, a full decomposition of change in ingredient cost expenditures was desired. The explicit changes in ingredient cost from year to year, relative to total cost in the first year, were calculated. These calculations used the amount of changes between years in ongoing products, the net change between adopted and abandoned products, and the amount of changes between years in new entities as individual component contributors and cumulatively as total change relative to the total cost in the first year. Examples of these calculations are included in Appendix A. Also, a summary of the relative magnitudes of the effects of inflation, utilization, prescription size, and product mix on the ongoing product ingredient cost, based on the results from the index approach, was included to provide overall factors affecting the ingredient cost changes.

All data management processes were done on either Microsoft Access 2000 or Microsoft Excel 2000, and all computations were done on either Microsoft Excel 2000 or SPSS 10.0 for Windows.

CHAPTER 4

RESULTS

Results will be presented in two main sections. The first section will present the results from the descriptive analyses. The second section will describe the results from the decomposition analyses.

Results from Descriptive Analysis

Table 4.1 shows the general description of the data from all diabetes patients who continuously enrolled in the health plan. The total drug ingredient cost, total number of prescriptions, and number of enrollees consistently increased across the study years. The total drug ingredient cost increased almost three-fold from the first to last years. The growth rate of the total ingredient costs consistently decreased from one period to another. It decreased from 43.7 percent in the first period to 19.8 percent in the last period. The total number of prescriptions inconsistently increased with double-digit rates across the study periods. The number of continuous enrollees also increased with different rates, which were consistent with the total number of prescriptions rates, across the study periods. The number of prescriptions per diabetes patient per year increased approximately one prescription in each period. The total ingredient cost per diabetes patient per year increased with diminishing rates across the study periods. The results suggested that increase in the number of diabetes patients could be a reason for the increase in the total ingredient cost. To remove the effects of variation in use by different enrollees, analyses then were restricted to the continuous enrollees who also continuously used anti-diabetic drugs.

Table 4.1 General Description of the Simulated Data from All Diabetes Patients who Continuously Enrolled in the Health Plan across the Study Years

	1996	$\%\Delta^1$	1997	$\%\Delta^2$	1998	$\%\Delta^3$	1999	$\%\Delta^4$	2000	$\%\Delta^5$
Total Drug Ingredient Cost	173,717	-	249,618	43.7	329,749	32.1	425,245	29.0	509,262	19.8
Total Numbers of Prescriptions	5,276	-	6,299	19.4	7,281	15.6	8,707	19.6	9,907	13.8
Number of Diabetes Patients	460	-	508	10.4	543	6.9	631	16.2	693	9.8
Number of Prescriptions per Diabetes Patient per Year	11	-	12	8.1	13	8.1	14	2.9	14	3.6
Total Drug Ingredient Cost per Diabetes Patient per Year	378	-	491	30.1	607	23.6	674	11.0	735	9.0

1, 2, 3, 4, 5 Percentage changes between 1996 and 1997, 1997 and 1998, 1998 and 1999, and 1999 and 2000, respectively.

Table 4.2 reports description of the data from continuous anti-diabetic drug users who continuously enrolled in the UHP across the study years. It includes total ingredient cost of prescription drugs, number of prescriptions, number of prescriptions per member per year, and total ingredient costs per member per year. The total drug ingredient cost more than doubled within the four-year period. Similar to the results in Table 4.1, the total ingredient costs of anti-diabetic drugs increased with diminishing rates. The total number of prescriptions continuously increased with different rates across the study years. The number of anti-diabetic drug users, who enrolled for the five-year study period, was 412. The number of prescriptions per diabetes patient per year consistently increased across the study periods. Even though trend of the number of prescriptions per diabetes patient per year of the continuous anti-diabetic drug users who continuously enrolled in the health plan was consistent with the result from all continuously enrolled diabetes patients, the intensity of the number of prescriptions per patient per year from the continuous enrollees who also continuously used anti-diabetic drugs was higher across the study years. The total ingredient cost per diabetes patient per year of the continuous anti-diabetic drug users who continuously enrolled in the health plan was higher than the total ingredient cost per diabetes patient per year of all continuously enrolled diabetes patients across the study years. Since the number of the continuous anti-diabetic drug users who continuously enrolled in the health plan was constant across the study years, the results suggested that the increase in the total drug ingredient cost per patient per year was primarily influenced by the number of prescriptions per patient per year.

Table 4.2 General Description of the Simulated Data from Continuous Anti-Diabetic Drug Users who Continuously Enrolled in the Health Plan across the Study Years

	1996	1997	1998	1999	2000
Total Drug Ingredient Cost	164,151	232,151	290,279	348,442	383,423.59
Total Drug Ingredient Cost per Diabetes Patient per Year[1]	398	564	705	846	930.64
%Δ	-	41.4[3]	25.0[4]	20.0[5]	10.0[6]
Total Numbers of Prescriptions	4,960	5,685	6,124	6,682	7,012
Number of Prescriptions per Diabetes Patient per Year[2]	12	14	15	16	17.02
%Δ	-	14.6[3]	7.7[4]	9.1[5]	4.9[6]

1, 2 Number of continuous anti-diabetic drug users who continuously enrolled in the health plan was 412.
3, 4, 5, 6 Percentage changes between 1996 and 1997, 1997 and 1998, 1998 and 1999, and 1999 and 2000, respectively.

Table 4.3 shows total drug ingredient costs across all products categorized into single-source and multiple-source product groups. The ingredient costs of the single-source products were the highest in the last three years and consistently increased in all years. The multiple-source innovator product costs were much higher than the costs of multiple-source generic products in all years. While the ingredient costs of the multiple-source generic products continuously increased in all years, the ingredient costs of the multiple-source innovator products slightly increased in the first period and then decreased in the later periods. The results suggested that some patients might switch from the multiple-source innovator products to either the single-source or the multiple-source generic products after the first period. This table also shows numbers of drug entities and numbers of NDCs across all product categories. A drug entity is a particular chemical entity with a specific strength and dosage form. Each drug entity can have several NDCs, depending on manufacturers, package size, etc. The results indicated cost and product mix changes of product types across the study periods. In particular, the numbers of drug entities for the single-source drug group increased each year and the multiple-source innovator group decreased each year. A similar pattern for NDCs in these two product groups was found in all years. There was a downward trend in the number of drug entities for the multiple-source generic products, but a sizeable increase in their number of NDCs between the years 1997 and 1998. Also, ratio of the NDC numbers to the number of drug entities was highest for the multiple-source generic products suggesting that the generic name products used in this period were produced by several manufacturers.

Table 4.3 Summary of the Simulated Drug Ingredient Costs across the Product Groups and Study Years

	1996 (N[1]) (n[2])	1997 (N[1]) (n[2])	1998 (N[1]) (n[2])	1999 (N[1]) (n[2])	2000 (N[1]) (n[2])
Single-source	43,050 (9) (9)	107,394 (13) (16)	179,420 (15) (22)	241,552 (25) (38)	278,478 (26) (40)
Multiple-source innovator	112,196 (15) (33)	113,297 (14) (26)	91,969 (12) (21)	84,249 (11) (17)	81,803 (9) (15)
Multiple-source generic	8,905 (13) (47)	11,461 (12) (45)	18,890 (11) (57)	22,641 (11) (55)	23,143 (11) (56)
Overall	164,151 (27) (89)	232,151 (31) (87)	290,279 (31) (100)	348,442 (40) (110)	383,424 (40) (111)

1 Numbers of drug entities
2 Numbers of products (unique NDC)

Before examining the effects of different factors influencing drug costs, the overall drug ingredient cost was explored. A summary of drug ingredient costs is shown in Table 4.4. The total ingredient cost was divided into the ingredient cost of the ongoing, adopted, abandoned, and new entity groups. For the ongoing, adopted and abandoned products, the ingredient costs also were broken into single-source, multiple-source innovator, and multiple-source generic product groups. The table also includes the percentages of total dollar amounts of drug ingredient costs for each group of products, indicating proportionately how different groups of products contributed to overall total ingredient costs. It is noteworthy that even though the second year of a period was the same as the first year of its consecutive period, the products might be categorized differently in each period. For instance, if a product was an ongoing product in the first period, but it was abandoned in the second year of the second period, it was then categorized as an abandoned product in the first year of the second period. However, the total ingredient cost was still the same in each year. This note also applies to any tables, which report the results on per period base.

The total ingredient costs of ongoing products were the highest amount in all periods. The total ingredient costs of ongoing products consistently increased across the study periods. All trends of the ingredient costs of the single-source products and multiple-source products under the ongoing product category were similar to the trends of the overall ingredient costs of those products shown in Table 4.3. The ingredient costs of the single-source ongoing products continuously increased in every period, except the last period. The ingredient costs of the multiple-source innovator products decreased across the study periods. Therefore, even though the ingredient cost of the single-source products

Table 4.4 Summary of Drug Ingredient Costs across the Product Groups and Study Years

	1996-1997		1997-1998		1998-1999		1999-2000	
	1996 (%[1])	1997 (%[1])	1997 (%[1])	1998 (%[1])	1998 (%[1])	1999 (%[1])	1999 (%[1])	2000 (%[1])
Ongoing Products	**161,457 (98.4)**	**199,872 (86.1)**	**203,694 (87.7)**	**217,738 (75.0)**	**287,959 (99.2)**	**330,654 (94.9)**	**336,995 (96.7)**	**298,548 (77.9)**
Single-source	42,988 (26.2)	76,326 (32.9)	80,894 (34.9)	108,691 (37.4)	179,420 (61.8)	224,805 (64.5)	231,195 (66.4)	197,002 (51.38)
Multiple-source innovator	110,937 (67.6)	113,014 (48.7)	112,092 (48.3)	91,969 (31.7)	90,041 (31.0)	84,113 (24.1)	83,489 (24.0)	79,910 (20.84)
Multiple-source generic	7,531 (4.6)	10,533 (4.5)	10,708 (4.6)	17,078 (5.9)	18,498 (6.4)	21,737 (6.2)	22,311 (6.4)	21,636 (5.6)
Adopted Products	-	**5,779 (2.5)**	-	**3,710 (1.3)**	-	**9,952 (2.9)**	-	**5,338 (1.4)**
Single-source	-	4,568 (2.0)	-	1,898 (0.7)	-	8,911 (2.6)	-	1,938 (0.5)
Multiple-source innovator	-	282 (0.1)	-	0 (0)	-	136.5 (0.04)	-	1,893 (0.5)
Multiple-source generic	-	928 (0.4)	-	1,812 (0.6)	-	904 (0.3)	-	1,507 (0.4)
Abandoned Products	**2,694 (1.6)**	-	**1,957 (0.8)**	-	**2,320 (0.8)**	-	**3,611 (1.0)**	-
Single-source	61.6 (0.04)	-	0 (0)	-	0 (0)	-	2521 (0.7)	-
Multiple-source innovator	1,259 (0.8)	-	1,204 (0.5)	-	1,928 (0.7)	-	760 (0.2)	-
Multiple-source generic	1,374 (0.8)	-	753 (0.3)	-	392 (0.1)	-	329 (0.1)	-
New Entities	**0 (0)**	**26,500 (11.4)**	**26,500 (11.4)**	**68,831 (23.7)**	**0 (0)**	**7,836 (2.3)**	**7,836 (2.3)**	**79,538 (20.7)**
Overall Totals	**164,151**	**232,151**	**232,151**	**290,279**	**290,279**	**348,442**	**348,442**	**383,424**

1 Percentage based on overall totals for each year

was lower than the multiple-source innovator products in the first two years, the ingredient cost of the single-source products became higher in the last three periods. The ingredient costs of the multiple-source generic ongoing products were relatively low, compared to the single-source and multiple-source innovator ongoing product ingredient costs. However, the ingredient cost of the multiple-source generic ongoing products consistently increased across the first three periods and slightly decreased in the last period. The adopted and abandoned products accounted for very small portions of the total ingredient costs across the study periods. Interestingly, the ingredient cost of the adopted product was always higher than the abandoned product ingredient cost in every period. The new entities had major impacts on the total ingredient costs.

In the first period, the new entity, Rezulin®, first appeared during in 1997, and its ingredient cost was $26,500, which was about 11 percent of the overall costs of year 1997. In the second period, the contribution of the new entities to the ingredient cost was $68,831 in 1998, up from $26,500 in 1997, more than two fold. In the third period, there were new entities, Actos® and Avandia®, in 1999. Their ingredient costs were still low in this period since it was only their introductory year. The results from the last period were very interesting. Even though the ingredient cost of the ongoing products was still the highest amount and percentage of the overall ingredient cost, it decreased $38,448 (from $336,995 to $298,548), mostly from a decrease in the single-source products of $34,193 (from $231,195 to $197,002). The increase of the new entity cost in the last period was $71,702 (from $7,836 to $79,538), which was almost a 10-fold increase. This increase had a major impact on the overall ingredient cost in the period.

Ongoing product cost change, adopted and abandoned product cost change, and new entity cost change were an approach to examine the effects of these different product groups on the overall ingredient cost change per period. The results are summarized in Table 4.5. Ongoing product cost change represents the effect of the changes of the ongoing products used on the overall change of the prescription drug ingredient cost in a period. Adopted and abandoned product cost change presents how adopted and abandoned products were mixed, in other words, it shows the changes of the ingredient costs from adding in adopted products and abandoned products used in the previous year (amount of change was equal to value of the adopted products in the second year of the period less value of abandoned products in the first year of the same period). The new entity cost change is similar to the ongoing product change mix, but since the new entities were the products that were launched into the market between the study period, and relatively expensive, they were analyzed separately. The total incremental changes fluctuated across the study periods. Mainly the cost changes of the single-source ongoing products and the additions of the new entities contributed to the changes in the prescription drug ingredient costs each period. In the last period, the new entity cost change provided all of the increase in the ingredient cost, primarily from Actos® and Avandia®, overcoming a total decrease in the ongoing product group, mainly from the removal of Rezulin® from the market.

Even though the number of enrollees was equal across all studied years, calculations based on per member per year of drug ingredient costs were done in order to be consistent with previous studies and make analysis easier. Table 4.6 shows the summary of drug ingredient costs per diabetes patient per year across the product groups and study years.

Table 4.5 Summary of Ongoing Product Cost Change, Adopted and Abandoned Product Cost Change, and New Entity Cost Change across the Product Groups and Study Periods

	1996-1997 (%[1])	1997-1998 (%[1])	1998-1999 (%[1])	1999-2000 (%[1])
Ongoing Products	**38,416 (56.5)**	**14,043 (24.2)**	**42,695 (73.4)**	**-38,448 (-109.9)**
Single-source	33,337 (49.0)	27,797 (47.8)	45,384 (78.0)	-34,193 (-97.8)
Multiple-source innovator	2,077 (3.1)	-20,123 (-34.6)	-5,928 (-10.2)	-3,579 (-10.2)
Multiple-source generic	3,001 (4.4)	6,370 (11.0)	3,239 (5.6)	-676 (-1.9)
Adopted-Abandoned Products[2]	**3,085 (4.5)**	**1,753 (3.0)**	**7,632 (13.1)**	**1,728 (4.9)**
Single-source	4,507 (6.6)	1,898 (3.3)	8,911 (15.3)	-583 (-1.7)
Multiple-source innovator	-976 (-1.4)	-1,204 (-2.1)	-1,791 (-3.1)	1,133 (3.2)
Multiple-source generic	-446 (-0.7)	1,059 (1.8)	512 (0.9)	1,178 (3.4)
New Entities	**26,500 (39.0)**	**42,332 (72.8)**	**7,836 (13.5)**	**71,702 (205.0)**
Total Incremental Change	**68,000**	**58,128**	**58,163**	**34,982**

1 Percentage of total incremental change

2 Adopted-Abandoned amounts are the net changes that result from subtracting amount for abandoned products in the first year from amount for adopted products in the second year.

Table 4.6 Summary of Drug Ingredient Costs per Diabetes Patient per Year across the Product Groups and Study Years

	1996-1997		1997-1998		1998-1999		1999-2000	
	1996	1997	1997	1998	1998	1999	1999	2000
Ongoing Products	**392**	**485**	**494**	**528**	**699**	**803**	**818**	**725**
Single-source	104	185	196	264	435	546	561	478
Multiple-source innovator	269	274	272	223	219	204	203	194
Multiple-source generic	18	26	26	41	45	53	54	53
Adopted Products	**-**	**14**	**-**	**9**	**-**	**24**	**-**	**13**
Single-source	-	11	-	5	-	22	-	5
Multiple-source innovator	-	1	-	0	-	0.3	-	5
Multiple-source generic	-	2	-	4	-	2	-	4
Abandoned Products	**7**	**-**	**5**	**-**	**6**	**-**	**9**	**-**
Single-source	0.2	-	0	-	0	-	6	-
Multiple-source innovator	3	-	3	-	5	-	2	-
Multiple-source generic	3	-	2	-	1	-	1	-
New Entities	**0**	**64**	**64**	**167**	**0**	**19**	**19**	**193**
Overall Totals	**398**	**563**	**563**	**705**	**705**	**846**	**846**	**931**

Since the denominators (number of enrollees, which was equal to 412) were constant, the trends were the same as the results from Table 4.4. The overall total ingredient costs per member per year continuously increased across all years. The ingredient costs per member per year for the ongoing products consistently increased in the first three periods, but decreased in the last period. However, the result showed the ingredient cost per member per year for the ongoing products in year 2000 was almost double that in 1996. The ingredient costs per member per year of the single-source and multiple-source generic products under the ongoing product category increased for all first three periods, but dropped in the last period. The cost per member per year of the multiple-source innovator products increased in the first period, then it diminished in later periods. The costs per member per year of the adopted and abandoned products inconsistently changed across years. Both of them had relatively low cost per member per year. An interesting result was that the ingredient costs per member per year for the new entities dramatically increased after their first year of introduction (from $64 in year 2 to $167 in year 3 and from $19 in year 4 to $193 in the last year).

To analyze prescription drug costs, there were several alternatives. The average cost per prescription was introduced to start a price and quantity explanation. The average weighted unit price represented the price component of the ingredient costs, and the prescription size and number of prescriptions represented the quantity component. The results of average cost per prescription are shown in Table 4.7, including the number of prescriptions.

Table 4.7 Summary of Average Drug Ingredient Costs per Prescription across the Product Groups and Study Years

	1996-1997		1997-1998		1998-1999		1999-2000	
	1996 (N[1])	1997 (N[1])	1997 (N[1])	1998 (N[1])	1998 (N[1])	1999 (N[1])	1999 (N[1])	2000 (N[1])
Ongoing Products	**33.34 (4,843)**	**37.40 (5,344)**	**37.63 (5,413)**	**39.35 (5,533)**	**47.72 (6,034)**	**51.58 (6,410)**	**51.55 (6,537)**	**47.51 (6,284)**
Single-source	37.45 (1,148)	43.49 (1,755)	45.02 (1,797)	48.35 (2,248)	65.94 (2,721)	71.32 (3,152)	71.36 (3,240)	64.70 (3,045)
Multiple-source innovator	35.53 (3,122)	39.02 (2,896)	38.99 (2,875)	41.15 (2,235)	40.95 (2,199)	42.44 (1,982)	42.49 (1,965)	41.68 (1,917)
Multiple-source generic	13.14 (573)	15.20 (693)	14.45 (741)	16.26 (1,050)	16.60 (1,114)	17.04 (1,276)	16.75 (1,332)	16.37 (1,322)
Adopted Products	-	**37.53 (154)**	-	**23.19 (160)**	-	**50.01 (199)**	-	**55.60 (96)**
Single-source	-	108.77 (42)	-	45.18 (42)	-	84.07 (106)	-	80.76 (24)
Multiple-source innovator	-	25.68 (11)	-	0 (0)	-	68.25 (2)	-	94.65 (20)
Multiple-source generic	-	9.19 (101)	-	15.36 (118)	-	9.93 (91)	-	28.98 (52)
Cutoff Products	**23.03 (117)**	-	**23.02 (85)**	-	**25.78 (90)**	-	**50.16 (72)**	-
Single-source	61.62 (1)	-	0 (0)	-	0 (0)	-	140.05 (18)	-
Multiple-source innovator	30.70 (41)	-	37.64 (32)	-	53.55 (36)	-	40.02 (19)	-
Multiple-source generic	18.32 (75)	-	14.20 (53)	-	7.26 (54)	-	9.40 (35)	-
New Entities	**0 (0)**	**141.71 (187)**	**141.71 (187)**	**159.70 (431)**	**0 (0)**	**107.34 (73)**	**107.34 (73)**	**125.85 (632)**
Overall Totals	**33.09 (4,960)**	**40.84 (5,685)**	**40.84 (5,685)**	**47.40 (6,124)**	**47.40 (6,124)**	**52.15 (6,682)**	**52.15 (6,682)**	**54.68 (7,012)**

1 Numbers of Prescriptions

The overall average cost per prescription and the overall numbers of prescriptions consistently increased across all years. The average cost per prescription and the numbers of prescriptions of overall ongoing products consistently increased, except the last period. A similar pattern occurred for the single-source and multiple-source generic ongoing products. The average prescription price increased, but the numbers of prescriptions for the multiple-source innovator products consistently decreased across all periods. The numbers of prescriptions for the adopted and abandoned products showed the multiple-source innovator products tended to be abandoned, while the single-source and multiple-source generic products were adopted. The results suggest that the multiple-source innovator products might be replaced by the multiple-source generic products and some patients may have switched from multiple-source innovator to single-source products. The new entities were the most expensive per prescription costs among the product types in all years, except for abandoned single-source drugs in the last period. Although their numbers of prescriptions were small, their costs per prescription were much higher than others.

Some specific results in the first and last periods show the impact that changes that one or a few products can have. In the first period, the average cost per prescription of adopted single-source products was quite high, mostly due to prescriptions for Glucophage®, an expensive product. In the last period, the average price of abandoned products was very high, due to the removal of Rezulin® from the market.

Table 4.8 shows the average unit price across the product groups and study years. The overall average unit prices consistently increased across periods. The average unit prices of the ongoing products increased consistently for single-source and multiple-source

Table 4.8 Summary of Average Weighted (by Quantity Used) Unit Price across the Product Groups and Study Years

	1996-1997		1997-1998		1998-1999		1999-2000	
	1996	1997	1997	1998	1998	1999	1999	2000
Ongoing Products	**0.68**	**0.72**	**0.73**	**0.71**	**0.88**	**0.92**	**0.91**	**0.85**
Single-source	0.52	0.61	0.64	0.68	0.99	1.05	1.04	0.95
Multiple-source innovator	0.94	1.09	1.12	1.54	1.57	1.96	1.97	2.18
Multiple-source generic	0.21	0.22	0.20	0.20	0.21	0.22	0.21	0.20
Adopted Products	**-**	**0.61**	**-**	**0.43**	**-**	**0.58**	**-**	**1.24**
Single-source	-	2.78	-	1.43	-	1.06	-	3.57
Multiple-source innovator	-	3.21	-	0	-	4.55	-	4.51
Multiple-source generic	-	0.12	-	0.25	-	0.10	-	0.45
Abandoned Products	**0.33**	**-**	**0.26**	**-**	**0.37**	**-**	**0.93**	**-**
Single-source	30.81	-	0	-	0	-	4.85	-
Multiple-source innovator	0.51	-	0.37	-	0.79	-	1.12	-
Multiple-source generic	0.25	-	0.18	-	0.10	-	0.12	-
New Entities	**0**	**3.75**	**3.75**	**3.64**	**0**	**3.12**	**3.12**	**3.29**
Overall Totals	**0.67**	**0.79**	**0.79**	**0.87**	**0.87**	**0.92**	**0.92**	**1.01**

innovator products, except for a drop for single-source products in the last period. The average unit prices of the adopted products were higher than the average unit prices of the abandoned products across the study periods. The average unit prices of the new entities were very high, compared to other product groups in the same periods.

There were several interesting results across the study periods. In the first period, the average unit price of the abandoned single-source products was very high due to a prescription for Glucophage®, which was an expensive product that was given up in 1997. The average unit prices for new entities were very high due to the average unit prices of Rezulin® in the first and second periods (with the drop in the second period due to lower strengths of Rezulin® prescriptions) and Actos® and Avandia® in the last two periods. The high average unit price of the abandoned single-source products in the last period was relatively high because Rezulin® was withdrawn from the market.

Among the ongoing products, the multiple-source innovator products seemed to be the highest average unit price in every period. This result was in conflict with common knowledge of price differences between the single-source and multiple-source innovator products, which was that the average unit price of single-source products was potentially higher. After reviewing the raw data, a lot of liquid dosage form products were found. The unit prices thus contained either price per tablet (or capsule) or price per milliliter. Therefore these various unit prices caused problematic comparisons. Even though the changes of prices per unit provided the inflation effect on the prescription drug ingredient costs, they might not be an appropriate unit when they were compared across product groups.

To make more comparable costs across product groups, average weighted cost per day was calculated and reported in Table 4.9. The overall average costs per day continuously increased in every period. The average costs per day of the ongoing products increased, except in the last period. Among ongoing products, the average cost per day of the single-source products was less than the average cost per day for the multiple-source innovator products for the first two periods and vice versa the last two periods. The average cost per day of the adopted products was higher than the average costs per day of abandoned products across all the study periods. The average costs per day of the new entities always were the highest among all product groups, reflecting the high costs of Rezulin®, Actos® and Avandia®.

The prescription size was a potentially confounding factor, which had an impact on the prescription drug costs, Table 4.10 shows the average prescription size across the product groups and study years. The overall average prescription size consistently increased slightly across the study periods, except the last period, resulting from relatively stable prescription sizes for the single-source products, decrease for the multiple-source innovator, and increase for the multiple-source generic products. While the average prescription size of the adopted and abandoned products inconsistently changed across the periods, the average prescription size of the new entities consistently increased after their introductory years.

Since the average cost per day was reported in this study, average day supply per prescription was then calculated and is shown in Table 4.11. The overall average day supply per prescription was generally stable across periods, ranging from 25.6 to 26.3. The average day supply per prescription of the ongoing products followed the same trend, with quite

Table 4.9 Summary of Average Weighted (by numbers of day supply) Cost per Day across the Product Groups and Study Years

	1996-1997		1997-1998		1998-1999		1999-2000	
	1996	1997	1997	1998	1998	1999	1999	2000
Ongoing Products	**1.31**	**1.45**	**1.46**	**1.52**	**1.82**	**1.98**	**1.97**	**1.87**
Single-source	1.27	1.51	1.57	1.68	2.27	2.49	2.51	2.31
Multiple-source innovator	1.53	1.69	1.70	1.99	1.99	2.16	2.17	2.26
Multiple-source generic	0.44	0.53	0.49	0.53	0.55	0.56	0.56	0.56
Adopted Products	**-**	**1.27**	**-**	**0.91**	**-**	**1.83**	**-**	**2.22**
Single-source	-	4.66	-	2.93	-	3.31	-	4.36
Multiple-source innovator	-	1.00	-	0	-	2.28	-	3.23
Multiple-source generic	-	0.28	-	0.53	-	0.33	-	1.10
Abandoned Products	**0.75**	**-**	**0.69**	**-**	**0.93**	**-**	**1.82**	**-**
Single-source	2.05	-	0	-	0	-	4.74	-
Multiple-source innovator	0.90	-	0.96	-	1.99	-	1.77	-
Multiple-source generic	0.63	-	0.47	-	0.26	-	0.32	-
New Entities	**0**	**4.63**	**4.63**	**5.03**	**0**	**3.50**	**3.50**	**4.14**
Overall Totals	**1.29**	**1.57**	**1.57**	**1.81**	**1.81**	**1.99**	**1.99**	**2.12**

Table 4.10 Summary of Average Prescription Size (Unit per Prescription) across the Product Groups and Study Years

	1996-1997		1997-1998		1998-1999		1999-2000	
	1996 (N[1])	1997 (N[1])	1997 (N[1])	1998 (N[1])	1998 (N[1])	1999 (N[1])	1999 (N[1])	2000 (N[1])
Ongoing Products	**49 (4,843)**	**52 (5,344)**	**52 (5,413)**	**55 (5,533)**	**54 (6,034)**	**56 (6,410)**	**57 (6,537)**	**56 (6,284)**
Single-source	72 (1,148)	71 (1,755)	70 (1,797)	72 (2,248)	67 (2,721)	68 (3,152)	69 (3,240)	68 (3,045)
Multiple-source innovator	38 (3,122)	36 (2,896)	35 (2,875)	27 (2,235)	26 (2,199)	22 (1,982)	22 (1,965)	19 (1,917)
Multiple-source generic	62 (573)	71 (693)	71 (741)	81 (1,050)	79 (1,114)	79 (1,276)	80 (1,332)	81 (1,322)
Adopted Products	-	**62 (154)**	-	**54 (160)**	-	**87 (199)**	-	**45 (96)**
Single-source	-	39 (42)	-	32 (42)	-	79 (106)	-	23 (24)
Multiple-source innovator	-	8 (11)	-	0 (0)	-	15 (2)	-	21 (20)
Multiple-source generic	-	77 (101)	-	62 (118)	-	97 (91)	-	64 (52)
Abandoned Products	**69 (117)**	-	**89 (85)**	-	**70 (90)**	-	**60 (72)**	-
Single-source	2 (1)	-	0 (0)	-	0 (0)	-	29 (18)	-
Multiple-source innovator	60 (41)	-	103 (32)	-	68 (36)	-	36 (19)	-
Multiple-source generic	74 (75)	-	80 (53)	-	71 (54)	-	77 (35)	-
New Entities	**0 (0)**	**38 (187)**	**38 (187)**	**44 (431)**	**0 (0)**	**34 (73)**	**34 (73)**	**38 (632)**
Overall Totals	**49 (4,960)**	**52 (5,685)**	**52 (5,685)**	**54 (6,124)**	**54 (6,124)**	**57 (6,682)**	**57 (6,682)**	**54 (7,012)**

1 Numbers of Prescriptions

Table 4.11 Summary of Average Day Supply per Prescription across the Product Groups and Study Years

	1996-1997		1997-1998		1998-1999		1999-2000	
	1996 (N[1])	1997 (N[1])	1997 (N[1])	1998 (N[1])	1998 (N[1])	1999 (N[1])	1999 (N[1])	2000 (N[1])
Ongoing Products	**25.5 (4,843)**	**25.7 (5,344)**	**25.7 (5,413)**	**25.9 (5,533)**	**26.2 (6,034)**	**26.1 (6,410)**	**26.1 (6,537)**	**25.4 (6,284)**
Single-source	29.6 (1,148)	28.9 (1,755)	28.7 (1,797)	28.9 (2,248)	29.1 (2,721)	28.6 (3,152)	28.5 (3,240)	28.0 (3,045)
Multiple-source innovator	23.2 (3,122)	23.1 (2,896)	22.9 (2,875)	20.7 (2,235)	20.6 (2,199)	19.6 (1,982)	19.6 (1,965)	18.4 (1,917)
Multiple-source generic	29.6 (573)	28.9 (693)	29.3 (741)	30.5 (1,050)	30.4 (1,114)	30.0 (1,276)	30.0 (1,332)	29.4 (1,322)
Adopted Products	-	**29.5 (154)**	-	**25.5 (160)**	-	**27.4 (199)**	-	**25.0 (96)**
Single-source	-	23.3 (42)	-	15.4 (42)	-	25.4 (106)	-	18.5 (24)
Multiple-source innovator	-	25.7 (11)	-	0 (0)	-	30.0 (2)	-	29.3 (20)
Multiple-source generic	-	32.5 (101)	-	29.1 (118)	-	29.76 (91)	-	26.3 (52)
Cutoff Products	**30.8 (117)**	-	**33.5 (85)**	-	**27.8 (90)**	-	**27.5 (72)**	-
Single-source	30 (1)	-	0 (0)	-	0 (0)	-	29.6 (18)	-
Multiple-source innovator	34.0 (41)	-	39.1 (32)	-	26.9 (36)	-	22.6 (19)	-
Multiple-source generic	29.1 (75)	-	30.1 (53)	-	28.4 (54)	-	29.1 (35)	-
New Entities	**0 (0)**	**30.6 (187)**	**30.6 (187)**	**31.7 (431)**	**0 (0)**	**30.7 (73)**	**30.7 (73)**	**30.4 (632)**
Overall Totals	**25.6 (4,960)**	**26.0 (5,685)**	**26.0 (5,685)**	**26.3 (6,124)**	**26.3 (6,124)**	**26.2 (6,682)**	**26.2 (6,682)**	**25.8 (7,012)**

1 Numbers of Prescriptions

consistent average day supplies for the single-source and multiple-source generic products, and a slight, but consistent decrease for the multiple-source innovator products.

Interestingly, the decrease in average prescription size for the ongoing multiple-source innovator products was in conflict with the change of the average cost per prescription increase, but consistent with the change of the average day supply. These results suggest that either more potent or otherwise more expensive products were used with a lower frequency of drug administration per day. The average days supply and the average cost per prescription of the multiple-source generic ongoing products barely changed, but the average prescription size tended to increase, suggesting lower strengths, but more frequent dosing, of the multiple-source generic products occurred across the periods.

Table 4.12 shows the numbers of NDCs of the product groups that were counted to give a general idea of the product mix effect. The overall numbers of NDCs rose from 87 to 111 from the first to last periods. Only the numbers of NDCs of the ongoing products and new entities consistently increased. The numbers of NDCs of the single-source and multiple-source generic ongoing products increased from the first to last periods, while the number of NDCs of the multiple-source innovator ongoing products diminished across the periods. During the same periods, the numbers of NDCs of the adopted and abandoned products inconsistently changed. These results reflected that there was some degree of product mix that occurred in the anti-diabetic agent utilization.

Two kinds of product mix effect were examined. One of them was strength mix. It is an impact on product mix effect from strengths used, in cases where products have more than one strength. It is a certain degree of mixing between more or less expensive strengths.

Table 4.12 Summary of the Number of Unique NDCs across the Product Groups and Study Periods

	1996-1997	1997-1998	1998-1999	1999-2000
Ongoing Products	**63**	**68**	**82**	**86**
Single-source	8	11	22	26
Multiple-source innovator	24	21	16	13
Multiple-source generic	31	36	44	47
Adopted Products	**19**	**27**	**19**	**13**
Single-source	3	6	7	2
Multiple-source innovator	2	0	1	2
Multiple-source generic	14	21	11	9
Abandoned Products	**26**	**14**	**18**	**15**
Single-source	1	0	0	3
Multiple-source innovator	9	5	5	4
Multiple-source generic	16	9	13	8
New Entities	**5**	**5**	**9**	**12**
Overall Totals	**87**	**100**	**110**	**111**

1 Unique Number of NDCs

Table 4.13 reports the numbers of prescriptions used, their percentages of total number of prescriptions of each product, and their costs per prescription. The table shows how each product in a product line was mixed. Some of these products were mixed interestingly among their strengths in term of use trends over time and in relation to their costs per prescription. There was evidence that the more expensive strength was more likely used as time progressed. For instance, Actos® was introduced in 1999. Even though only two years of utilization were shown, Actos® 45 mg that had more expensive cost per prescription grew at a higher rate than other strengths. Similarly, this evidence also occurred for a number of products such as Amaryl®, Glucophage®, Glucotrol®, Glyburide®, Glynase®, and Precose®.

The strength mix was examined further by calculating the average milligram strength of each drug in each year, and the result is shown in Table 4.14. Several products with more than one strength had changes in both direction and magnitude in average milligram strength for each period. Only a few products showed consistently positive increases and with widely varying percentage changes.

Therapeutic mix is an impact of product mix effect from shifting in utilization to more or less expensive therapeutic classes within anti-diabetic drugs. Table 4.15 shows the number of prescription used in each therapeutic category of anti-diabetic drugs, their percentage of total prescriptions per year, and their average cost per prescription. There were eight therapeutic categories, based on their GPI. Only biguanides and thiazolidinedione had consistent increase in the percentage of prescriptions across periods. The mixed insulin's percentages decreased across the periods, while the percentage of numbers of prescriptions of sulfonyluria group increased in the first period, and then it diminished for the later periods.

Table 4.13 Summary of Number of Prescription Shares, and Average Cost per Prescription for Products with More Than One Strength across the Study Years

	1996			1997			1998			1999			2000		
	#Rx	%[1]	C/Rx[2]	#Rx	%[1]	C/Rx[2]	#Rx	%[1]	C/Rx[2]	#Rx	%[1]	C/Rx[2]	#Rx	%[1]	C/Rx[2]
Actos															
15 mg	0	0	0	0	0	0	0	0	0	5	35.7	82.65	70	30.3	107.46
30 mg	0	0	0	0	0	0	0	0	0	4	28.6	132.33	57	24.7	138.72
45 mg	0	0	0	0	0	0	0	0	0	5	35.7	143.55	104	45.0	150.02
Amaryl															
1 mg	0	0	0	0	0	0	2	2.1	15.14	8	3.9	22.69	11	4.5	23.12
2 mg	0	0	0	12	85.7	15.15	45	46.4	15.93	66	31.7	16.42	62	25.2	16.74
4 mg	0	0	0	2	14.3	20.73	50	51.5	29.46	134	64.4	33.97	173	70.3	35.54
Avandia															
2 mg	0	0	0	0	0	0	0	0	0	3	5.1	105.00	9	2.2	132.73
4 mg	0	0	0	0	0	0	0	0	0	37	62.7	84.50	275	68.6	112.77
8 mg	0	0	0	0	0	0	0	0	0	19	32.2	143.91	117	29.2	139.29
Chlorpropamide															
100 mg	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
250 mg	26	100	19.18	20	100.0	24.93	10	100	38.91	12	100	25.60	12	100.0	19.2
Diabeta															
1.25 mg	5	0.6	13.58	6	0.9	18.13	0	0	0	0	0	0	0	0	0
2.5 mg	121	14.2	12.52	99	15.0	14.32	39	24.4	18.47	12	23.5	11.58	11	55	11.58
5 mg	724	85.2	47.52	556	84.1	51.61	121	75.6	56.78	39	76.5	61.47	9	45	83.39
Glipizide															
5 mg	151	57.9	2.33	111	46.3	2.57	105	54.4	3.52	129	62.0	3.79	127	58.3	4.13
10 mg	110	42.1	6.85	129	53.8	5.70	88	45.6	4.95	79	38.0	5.51	91	41.7	5.50
Glucophage															
500 mg	672	91.1	41.55	899	85.4	47.10	1,048	80.9	54.28	1,225	77.4	62.62	1,101	65.1	68.39
850 mg	66	8.9	58.36	154	14.6	68.68	247	19.1	69.85	292	18.5	78.81	372	22.0	80.25
1000 mg	0	0	0	0	0	0	0	0	0	65	4.1	81.27	218	12.9	78.32
Glucotrol															
5 mg	27	61.4	30.93	10	45.5	72.60	0	0	0	0	0	0	0	0	0
10 mg	17	38.6	80.08	12	54.5	83.28	1	100.0	85.50	0	0	0	0	0	0

1 Percentage of number of prescriptions of each strength for each product
2 Cost per prescription

	1996			1997			1998			1999			2000		
	#Rx	%[1]	C/Rx[2]	#Rx	%[1]	C/Rx[2]	#Rx	%[1]	C/Rx[2]	#Rx	%[1]	C/Rx[2]	#Rx	%[1]	C/Rx[2]
Glucotrol XL															
2.5 mg	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5 mg	157	50.6	15.35	198	46.6	15.24	176	37.5	14.74	153	34.9	16.28	128	29.0	14.68
10 mg	153	49.4	31.79	227	53.4	31.76	293	62.5	32.14	286	65.1	34.90	313	71.0	38.58
Glyburide															
1.25 mg	2	1.2	2.83	0	0	0	6	0.8	5.66	14	1.7	5.06	17	2.2	5.99
2.5 mg	25	15.0	3.11	45	13.2	5.77	77	11.0	6.85	94	11.5	6.04	107	13.6	5.34
5 mg	140	83.8	10.12	296	86.8	10.90	620	88.2	11.14	713	86.8	11.33	661	84.2	11.52
Glyburide Micronized															
1.5 mg															
3 mg	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6 mg	58	100.0	6.03	65	100.0	6.53	73	57.0	6.54	79	47.6	8.00	105	59.3	7.64
	0	0	0	0	0	0	55	43.0	14.49	87	52.4	16.49	72	40.7	17.91
Glynase															
1.5 mg	12	4.0	9.74	12	4.2	9.75	13	6.2	10.62	12	15.8	12.60	11	33.3	13.74
3 mg	126	42.6	30.66	100	34.8	22.54	74	35.4	29.61	11	14.5	34.85	0	0	0
6 mg	158	53.4	45.72	175	61.0	53.16	122	58.4	64.05	53	69.7	70.02	22	66.7	90.95
Micronase															
2.5 mg	3	20.0	19.90	0	0	0	0	0	0	0	0	0	0	0	0
5 mg	12	80.0	45.27	0	0	0	0	0	0	0	0	0	0	0	0
Prandin															
0.5 mg	0	0	0	0	0	0	0	0	0	13	40.6	54.21	3	15.8	61.50
1 mg	0	0	0	0	0	0	0	0	0	7	21.9	87.07	5	26.3	149.20
2 mg	0	0	0	0	0	0	0	0	0	12	37.5	142.35	11	57.9	187.88
Precose															
25 mg	0	0	0	0	0	0	1	2.2	41.05	5	14.3	57.15	5	20.8	60.03
50 mg	30	85.7	24.40	37	84.1	33.03	39	84.8	54.88	10	28.6	84.30	9	37.5	70.66
100 mg	5	14.3	52.92	7	15.9	52.92	6	13.0	54.88	20	57.1	49.13	10	41.7	46.53
Rezulin															
200 mg	0	0	0	87	46.5	126.67	149	34.5	147.96	144	32.6	145.98	21	29.2	162.62
300 mg	0	0	0	4	2.1	190.47	71	16.5	184.34	129	29.2	179.63	25	34.7	179.28
400mg	0	0	0	96	51.3	153.31	211	49.0	159.70	168	38.1	157.07	26	36.1	157.33
Tolazamide															
250 mg	20	62.5	8.03	20	66.7	9.24	31	100	9.44	33	100.0	9.64	34	100.0	9.72
500 mg	12	37.5	6.37	10	33.3	6.37	0	0	0	0	0	0	0	0	0

1 Percentage of number of prescriptions of each strength for each product

2 Cost per prescription

Table 4.14 Summary of Average Milligram Strength[1] across the Products and Study Years

	1996		1997		1998		1999		2000	
	Average mg Strength	% Change	Average mg Strength	% Change[2]	Average mg Strength	% Change[3]	Average mg Strength	% Change[4]	Average mg Strength	% Change[5]
Actos	-	-	-	-	-	-	30.0	-	32.2	7.4
Amaryl	-	-	2.3	-	3.0	31.4	3.3	8.0	3.4	3.4
Avandia	-	-	-	-	-	-	5.2	-	5.1	-1.2
Chlorpropamide	250.0	-	250.0	0	250.0	0	250.0	0	250.0	0
Diabeta	4.6	-	4.6	-0.7	4.4	-4.4	4.4	0.5	3.6	-17.8
Glipizide	7.1	-	7.7	8.2	7.3	-5.3	6.9	-5.2	7.1	2.7
Glucophage	531.3	-	551.2	3.7	566.8	2.8	585.1	3.2	641.5	9.3
Glucotrol	6.9	-	7.7	11.5	10.0	29.4	-	-	-	-
Glucotrol XL	7.5	-	7.7	2.7	8.1	5.9	8.3	1.7	8.6	3.5
Glyburide	4.6	-	4.7	2.0	4.7	0.4	4.7	-0.9	4.6	-1.5
Glyburide Micronized	3.0	-	3.0	0	4.3	43.0	4.6	6.5	4.2	-7.7
Glynase	4.5	-	4.8	5.0	4.7	-2.3	4.9	4.1	4.5	-7.3
Micronase	4.5	-	-	-	-	-	-	-	-	-
Prandin	-	-	-	-	-	-	1.2	-	1.5	28.0
Precose	57.1	-	58.0	1.4	56.0	-3.4	75.0	34.0	65.6	-12.5
Rezulin	-	-	304.8	-	314.4	3.1	305.4	-2.9	306.9	0.5
Tolazamide	343.8	-	333.3	-3.0	250.0	-25.0	250.0	0	250.0	0

1 Sum of product of number of prescriptions and milligram strengths and divided by total number of prescriptions
2, 3, 4, 5 Percent changes between 1997 and 1998, 1998 and 9999, 1999 and 2000, respectively.

Table 4.15 Summary of Therapeutic Mix across the Therapeutic Categories and Study Years

	1996			1997			1998			1999			2000		
	#Rx[1]	%[2]	C/Rx[3]	#Rx[1]	%[2]	C/Rx[3]	#Rx[1]	%[2]	C/Rx[3]	#Rx[1]	%[2]	C/Rx[3]	#Rx[1]	%[2]	C/Rx[3]
Alpha-Glucosidase Inhibitors	35	0.7	28.48	44	0.8	36.19	46	0.8	52.12	35	0.5	60.32	24	0.3	58.39
Biguanides	738	14.9	43.06	1,053	18.5	50.25	1,295	21.2	57.25	1,582	23.7	66.37	1,691	24.1	72.28
Human Insulin	1,896	38.2	33.16	2,079	36.6	40.22	2,193	35.8	43.81	2,426	36.3	47.68	2,565	36.6	49.44
Meglitinides	0	0	0	0	0	0	0	0	0	32	0.5	94.45	19	0.3	157.75
Mixed Insulin	180	3.6	30.48	166	2.9	32.31	109	1.8	37.82	21	0.3	49.86	2	0.03	54.62
Sulfonylureas	738	14.9	29.56	2,111	37.1	28.38	2,001	32.7	21.13	2,015	30.2	18.57	1,967	28.1	17.92
Thiazolidinedione	0	0	0	187	3.3	141.71	431	7.0	159.70	514	7.7	152.56	704	10.0	130.01
Others	38	0.8	46.13	45	0.8	49.82	49	0.8	49.68	57	0.9	101.02	40	0.6	77.22

1 Numbers of Prescriptions
2 Percentage of numbers of prescriptions of each particular products
3 Average cost per prescription

The average costs per prescription of the biguanides and thiazolidinedione were relatively expensive, while the average costs per prescription of the mixed insulin and sulfonyluria groups were less expensive, compared to other therapeutic groups. Other therapeutic groups had stable percentages of numbers of prescriptions or slightly changed across the periods.

Results from Decomposition Analysis

The theory of index numbers was introduced to decompose the effects of inflation, prescription size, product mix, and utilization on the ongoing products ingredient cost, which were the major components of the drug ingredient costs. Also, the ongoing products had price and quantity information for two consecutive years of a period, which was needed for index calculation. The Laspeyres index, Tornqvist discrete approximation to the Divisia index, and refined Divisia index were used to decompose the cost per member per year of the ongoing products and the results are presented in Table 4.16. The first year and the second year of each period were used as time 0 and time T, respectively, to compute the indexes. The index numbers captured changes of the effects between the first and second years. Therefore, the indexes can be interpreted as percentages of changes of all effects from the first year to the second year. For instance, if an index is 1.2000, this index can be interpreted as 20 percent increase from the first year to the second year. It is noteworthy that since the Laspeyres index used the additive approach, the summation of all effects provided the total change in cost per patient per year, while the multiplicative approach was applied to the Tornqvist approximation to the Divisia index and refined Divisia index, the product of all effects gave the total change in cost per patient per year. The overall results show that even though the magnitudes of all effects were not exactly the same, they were close and had

Table 4.16 Summary of Indexes of All Ongoing Products across the Study Periods

	1996-1997	1997-1998	1998-1999	1999-2000
Laspeyres Index				
Prescription Size Effect	1.0202	1.0430	1.0017	0.9913
Inflation Effect	1.0725	1.0569	1.0737	1.0507
Product Mix Effect	1.0119	0.9633	0.9945	0.8899
Utilization Effect	1.1034	1.0222	1.0623	0.9613
Residuals	1.0299	0.9835	1.0160	0.9927
Torqvist Divisia Index				
Prescription Size Effect	1.0305	1.0370	1.0091	0.9830
Inflation Effect	1.0705	1.0569	1.0741	1.0547
Product Mix Effect	1.0399	0.9410	0.9981	0.8580
Utilization Effect	1.1034	1.0222	1.0623	0.9613
Residuals	0.9779	1.0138	0.9992	1.0360
Refined Divisia Index				
Prescription Size Effect	1.0277	1.0364	1.0074	0.9839
Inflation Effect	1.0710	1.0575	1.0728	1.0553
Product Mix Effect	1.0193	0.9541	1.0001	0.8876
Utilization Effect	1.1034	1.0222	1.0623	0.9613
Residuals	1.0000	1.0000	1.0000	1.0000
Total Cost per Diabetes Patient per Year Change	**1.2379**[1]	**1.0689**[1]	**1.1482**[1]	**0.8859**[1]

1 The results were calculated by adding up all effects for Laspeyres index and by multiplying all affects, including residuals, for refined Divisia and Torqvist Divisia indexes.

similar relative trends for all methods used. In other words, both additive and multiplicative approaches or all three indexes provided similar trends of all effects' movements. However, the Laspeyres and Tornqvist approximation to the Divisia indexes contained various magnitudes of residuals, which were not easily interpreted, all over the periods.

The index results can be viewed across the periods or within each period. Looking across periods from Table 4.16, the indexes indicated that the prescription size effect inconsistently increased in the first three periods, but decreased in the last period. The inflation effect was the only effect that had high positive magnitude (about five to seven percent) across all periods. The product mix was the most fluctuating effect across the periods. It was positive in the first period, negative in the second and last periods, and effectively neutral in the third period. The utilization effect had relatively high magnitude across the periods. It inconsistently increased across the first three periods, but decreased in the last period.

Examining trends within periods reveals that in the first period, all effects were positive yielding nearly 24 percent total increase for the period. The inflation and utilization effects were the major influences. The positive product mix result suggested that either more expensive product use increased or less expensive product use decreased. In the second period, the inflation was still the major effect, but it was offset by the negative product mix effect, yielding quite relatively lower total change. The negative product mix effect implied that either expensive product use decreased or less expensive product use increased in this period. The result from the third period was similar to the result from the first period, but not quite as strong for a combined total effect. Finally, the product mix was highly negative in the last period because of Rezulin® removal, combined with a negative utilization effect yielded a negative percentage overall total change.

The new ongoing products were not products launched during the analyzed period (which were defined as new entities in this study), but they were the ongoing products, which were launched within five years before a particular period. The effects from new ongoing products were expected to be important because of their diffusion period in the early years after being launched. All new ongoing products were dropped from the working file in order to examine their impact through all effects on the total cost per diabetes patient per year by examining the differences between the indexes from overall ongoing products and the old ongoing products. The results for the effect changes of the old ongoing products are presented in Table 4.17. Inflation was the only effect that still was highly positive across the periods. The effect of prescription size was positive in the first two periods, and then it was negative in the other periods. The product mix and utilization effects were negative across all periods. The result suggests that the ongoing products that were launched more than five years were less likely used, even though they were still expensive.

Table 4.18 summarizes the impact of the new ongoing products contributing to all effects, which came from the differences between the results from Table 4.16 and 4.17. Across the first three study periods, the new ongoing products enhanced the product mix and utilization effects, while their contribution on the inflation and prescription size effects was inconsistent. The results suggested that the new ongoing products, which were the ongoing products launched within five years before the analyzed periods, were a major part of the

Table 4.17 Summary of Indexes of Old Ongoing Products across the Study Periods

	1996-1997	1997-1998	1998-1999	1999-2000
Laspeyres Index				
Prescription Size Effect	1.0250	1.0792	0.9908	0.9747
Inflation Effect	1.0803	1.0504	1.0784	1.0437
Product Mix Effect	0.9485	0.8246	0.9593	0.9584
Utilization Effect	0.9871	0.9290	0.9982	0.9812
Residuals	1.0138	0.9903	0.9865	0.9940
Total Cost per Diabetes Patient per Year Change[1]	**1.0547[1]**	**0.8735[1]**	**1.0132[1]**	**0.9520[1]**

1 The results were calculated by adding up all effects for Laspeyres index.

Table 4.18 Summary of the Effects from New Ongoing Products across the Study Periods[1]

	1996-1997	1997-1998	1998-1999	1999-2000
Laspeyres Index				
Prescription Size Effect	0.9952	0.9638	1.0109	1.0166
Inflation Effect	0.9922	1.0065	0.9953	1.0070
Product Mix Effect	1.0634	1.1387	1.0352	0.9315
Utilization Effect	1.1163	1.0932	1.0641	0.9801
Residuals	1.0161	0.9932	1.0295	1.1309
Total Cost per Diabetes Patient per Year Change	**1.1832**[2]	**1.1954**[2]	**1.1350**[2]	**1.0661**[2]

1 These indexes were evaluated by subtracting the indexes of old ongoing products from the indexes of all ongoing products.
2 Total cost per diabetes patient per year change after including new ongoing products

increase in the total ingredient cost. In the first period, after deleting the new ongoing products, the total cost per patient per year change was lower by 18 percent (from 23.8 to 5.5 percent). The results showed the new ongoing products increased product mix and utilization change effects about 6 and 12 percent, respectively, while they decreased the price and prescription size effects one percent or less. In the second period, the new ongoing products increased the total cost change per patient per year from the old ongoing products about 20 percent (from -12.7 to 6.9 percent). All indexes show that the new ongoing products had the effects of inflation, product mix, and utilization changes increase by 0.7, 14, and 9 percent, respectively. Having new ongoing products decreased the effects of prescription size change about four percent in this period. In the third period, after adding the new ongoing products together with the old ongoing products, the total cost per patient per year change increased by 14 percent (from 1.3 to 14.8 percent). All indexes indicated there was a slight change in inflation effect, while there were approximately one, four, and six percent for the effects of prescription size, product mix and utilization changes, respectively. In the last period, the new ongoing products increased the total cost per patient per year change by seven percent (from -11.4 to -4.8 percent). All index results agreed that the new ongoing products increased the price and prescription size change effects by one and two percent, respectively, while they decreased the effects of product mix and utilization changes almost 10 and 2 percent, respectively. Rezulin® played an important role in the last period. Since Rezulin® was removed in early 2000, its utilization decreased. It highly reduced the product mix and utilization effects on all ongoing products in the last period. After dropping the new ongoing products, which also included some Rezulin® use earlier in the period before it was removed, it then made more negative effects of product mix and utilization.

The full decomposition of change in total cost per patient per year are summarized in Table 4.19. They were composed of the effects from the ongoing products (both old and new ongoing products), adopted and abandoned products, and new entities. Total cost per patient per year increased with double-digit percentages, but with diminishing rates across the studied periods. The relative effect of the ongoing products on the total cost change per patient per year inconsistently increased in the first three periods and decreased in the last period. The effects from adopted and abandoned products were always minimum across all periods. The effect of the new entities consistently increased across the study periods.

Since the refined Divisia index contained no residual, which was difficult to interpret, it was chosen to present the summary of the composition of the effects from the ongoing products. Because the refined Divisia index approach is a multiplicative method, multiplying the effects of price, prescription size, product mix, and utilization changes provides the overall effect from the ongoing products. However, no matter which index above was selected in this study, they should give similar trends. It is noteworthy that the effect of the ongoing products on the total cost change per patient per year in the full decomposition is different from the percentage change of the ongoing product ingredient cost per patient per year presented by the index results. The effect of the ongoing products on the total cost change per patient per year was computed based on the total cost per patient per year of the first year of each period, while the percentage change of the ongoing product ingredient cost

Table 4.19 Summary of the Decomposition of All Effects on the Changes of Diabetic Drug Cost per Patient per Year

	1996-1997	1997-1998	1998-1999	1999-2000
Ongoing Products[1]	23.40%	6.05%	14.71%	-11.03%
Adopted and Abandoned Products[1]	1.88%	0.76%	2.63%	0.50%
New Entities[1]	16.14%	18.23%	2.70%	20.58%
Total Cost Change per Patient per Year[2]	**41.43%**	**25.04%**	**20.04%**	**10.04%**
Ongoing Product Cost Change per Patient per Year[3]	**23.79%**	**6.89%**	**14.82%**	**-11.41%**
Prescription Size	2.77%	3.64%	0.74%	-1.61%
Inflation	7.10%	5.75%	7.28%	5.53%
Product Mix	1.93%	-4.59%	0.01%	-11.24%
Utilization	10.34%	2.22%	6.23%	-3.87%

1 This percentage was based on the total cost per patient per year of the first year in each period.
2 Total cost change per patient per year is the accumulated sum of overall ongoing products, adopted and abandoned products, and new entities.
3 This percentage was based on the ongoing product cost per patient per year of the first year in each period. All effects were factored out by using refined Divisia Index. The total for ongoing products represents the cumulative multiplicative effects.

per patient per year was calculated based on only the ingredient cost per member per year of the ongoing products in the first year of each period.

CHAPTER 5

DISCUSSIONS

This chapter will be composed of three major sections. The first section will provide a discussion of the descriptive analysis. The second section will discuss the results from decomposition analysis. Finally, the limitations of the study will be provided.

Discussion of Descriptive Analysis Results

An analysis was done on simulated data based on claims from all diabetes patients who continuously enrolled in the health plan across the study periods to show descriptive information. The results showed that there was evidence of the enrollee mix effect, which was not intended to be examined in this study. Therefore, only continuous anti-diabetic drug users who were continuous enrollees were further analyzed.

Table 4.2 showed that the total drug ingredient costs from the continuous anti-diabetic drug users, who were continuous enrollees, gradually increased across the study years, as well as total numbers of prescriptions, while the number of continuous diabetic drug users was constant or, in other words, the effect from population number changes was controlled. The increasing rates of total drug ingredient cost per member per year (PMPY) had been consistently diminishing across the periods, while total number of prescriptions PMPY had inconsistent increasing rates. Interestingly, total ingredient cost and total number of prescriptions increased more than 130 and 40 percent, respectively, in five years. This result reflected that one of the reasons of the increase in total ingredient cost was an effect from anti-diabetic drug utilization. This reason was consistent with American Diabetes Association's guideline because it suggested patients may have received multiple drugs or higher doses.

The effects from product types, single-source, multiple-source innovator, and multiple-source generic products, on the increase in total ingredient costs were summarized in Table 4.3. The increase in total ingredient costs across the study periods was attributable to the interaction between the increase in single-source and multiple-source generic product ingredient costs, and the decrease in multiple-source innovator product ingredient costs. This result could be partly explained by the distribution change of numbers of drug entities and numbers of unique NDCs. Both number of drug entities and unique NDCs for single-source products increased, while the number of drug entities and unique NDCs for multiple-source innovator products decreased across the periods. The number of multiple-source generic drug entities barely changed, while the number of unique NDCs increased across the periods. When either the number of NDCs or number of drug entities for a product type increased, its ingredient cost potentially increased and vise versa. The results were an indication of product mix effect.

Various product groups were defined and examined for their ingredient costs to show how ingredient costs of each product type contributed to overall total ingredient costs across the study periods. Table 4.4 summarized drug ingredient costs across the product groups and study years. Ongoing products were always the highest ingredient costs among those groups. The ingredient costs of ongoing products were primarily attributable to the single-source and multiple-source innovator products. In fact, the ingredient cost of the multiple-source innovator products was higher than the single-source ingredient cost in the first two years of the study periods. Another interesting result from this table was the ingredient cost of the new entities. Their ingredient costs dramatically arose after their introductory years. These results could be primarily explained by the role of the new entities. Rezulin® and Prandin® were introduced in 1997. Even though Prandin® was introduced at the same time as Rezulin®, it had not been used until 1999, and had very low volume, compared to Rezulin®. Therefore, Rezulin® played an important role after its introductory year in 1997. Its ingredient cost increased almost 160 percent (from $26,500 to $68,831) in the second study period. After this period, Rezulin® was incorporated into the single-source product under the ongoing product category. Then the ingredient cost of single-source products became higher than the multiple-source innovator ingredient cost. This influence also was confirmed when Rezulin® was withdrawn from the market in the year 2000, the ingredient cost of the single-source ongoing products decreased in the last period. Actos® and Avandia®, which were introduced in 1999, tended to play the same role as Rezulin® in the last period. It increased the ingredient cost more than $70,000 (from $7,836 to $79,438). Even though the ingredient cost of ongoing products decreased due to Rezulin® withdrawal, it was offset by the increase in the new entity ingredient cost. Therefore, the overall ingredient costs still rose in the last period.

The average drug ingredient cost per prescription and number of prescriptions across the product groups and study years were summarized in Table 4.7. The average weighted unit price and the average prescription size across all product groups and study years from Table 4.8 and 4.9, respectively, were presented to provide some detail about an "average" prescription. For the ongoing products, the first three periods shared several common trends. The average ingredient cost per prescription consistently increased in the first three periods. The average cost per prescription of all subgroups in the ongoing products consistently rose across these periods. Two components, the unit price and prescription size, of the average cost per prescription were used to explain the result. An increase in the average weighted unit prices was found across these periods. This result followed a fact that drug prices generally increased across time. The number of units per prescription or prescription size was slightly different across the first three periods. In the first period, the prescription size of the single-source and multiple-source innovator products decreased a little. Only the prescription size of the multiple-source innovator products decreased in the second period, while both multiple-source innovator and generic products had a decrease in their prescription size in the third period. The effect from price change was potentially higher than the prescription size change effect in the ongoing product group across the first three periods.

In the last period, the average cost per prescription of the ongoing products decreased. This result was attributable to a large decrease in the average cost per prescription of the single-source products, and slight decrease in the average cost per prescription of the multiple-source innovator and generic products. The decrease in the average cost per prescription of the single-source ongoing products was due to a decrease in both their average weighted unit price and average prescription size. The decrease in average cost per prescription of the multiple-source innovator products was primarily attributable to the decrease in their prescription size since their average weighted unit price was found to increase. In contrast, the decrease in the average weighted unit price was potentially attributed to the decrease in the average cost per prescription of the multiple-source generic products more than their average prescription size effect since an increase in the prescription size was found.

Even though costs from the adopted and abandoned products were minimal among all product groups, an interesting result was found that the average cost per prescription of the adopted products were higher than the average cost per prescription of the abandoned products across all periods. This also enhanced the increase in the overall average cost per prescription. After considering the average weighted unit price, more expensive products were more likely adopted than abandoned. The higher average cost per prescription of the adopted products was primarily due to higher average unit price because their average prescription size either increased or decreased across the periods.

The average cost per prescription of the new entities was incredibly high, compared to others. It also greatly increased after their introductory year. Interestingly, their average prescription size was not far apart from the average of other groups, but their average weighted unit price was relatively high.

Besides the average cost per prescription information, Table 4.7 included the number of prescriptions across the product groups and study years. This result also helped in explaining the average cost per prescription. While the numbers of prescriptions of the single-source and multiple-source generic ongoing products continuously increased, the number of prescriptions of the multiple-source innovator ongoing products consistently decreased in the first three periods. An interesting result of the change of number of prescriptions among the ongoing products was that the increase in number of prescriptions for the single-source products was higher than in the number of prescriptions for the multiple-source generic products. In other words, the multiple-source innovator ongoing product utilization was likely replaced by using single-source ongoing products, which were relatively expensive among the ongoing products. Then the numbers of prescriptions of all groups in the ongoing products decreased in the last period. Similar to their cost change, the number of prescriptions of the new entities highly increased after their introductory years.

After putting the results from average cost per prescription, average weighted unit price, average prescription size, and the distribution of numbers of prescription across the product groups and study years together, changes in all periods were concluded. In the first three periods, the increase in the average cost per prescription of the ongoing products was largely attributable to the increase in utilization of more expensive average cost per prescription products in the ongoing product subgroup, which were the single-source products. There also was evidence of higher utilization of the multiple-source generic products, which were cheaper products, but it was relatively small, compared to the increase in single-source product and new entity utilization. This result could be explained by either some patients switched from using the multiple-source innovator products to the single-source products or new entities or some of them had more intensive anti-diabetic drug utilization, especially on the single-source product or new entities. In the last period, since Rezulin®, which was a very expensive product, was withdrawn from the market, it decreased average cost per prescription, average weighted unit price, and numbers of prescriptions of the single-source ongoing products. However, since there were two new entities, Actos® and

Avandia® in the last period, their costs and utilization then offset the effect from Rezulin® withdrawal. Therefore the overall average cost per prescription, average weighted price, and numbers of prescriptions still increased in the last period.

The product mix effect was a relatively new factor in the previous studies, compared to the effects of inflation, prescription size, and utilization. A kind of product mix effect was strength mix. Strength mix explains the increases or decreases in overall cost due to switches in utilization to more or less expensive strengths. Across the study periods, the evidence of high utilization of more expensive cost per prescription strengths was found in several products. Average milligram strengths were calculated by gathering the product of number of prescriptions and strengths, and dividing by total number of prescriptions. There were interesting product lines, which showed the impact of strength mix. The positive changes meant the proportion of higher strength prescriptions was higher than the proportion of lower strength prescriptions. Basically, the higher strengths had higher average cost per prescription, which might eventually increase total ingredient costs rather than decrease them. In the first period, a number of products had positive percentage changes of average milligram strength, while only two products, Diabeta® and Tolazamide® had slightly negative percentage change. In the second period, one more product turned into negative strength mix and the previous negative average milligram strength products became more negative changes. In the third period, there were slightly negative percentage changes for three products, Glipizide®, Glyburide®, and Rezulin®, while many products had positive percentage changes with high magnitude. In the last period, the numbers of products that had negative percentage changes considerably increased. Evidently the results showed various degree of strength mix across the periods, which subsequently affected the total ingredient costs.

Therapeutic mix is the utilization of more or less expensive drugs within a therapy class, which is anti-diabetic agent in this study. Based on the number of prescriptions used, there were three large groups used, which were insulin, biguanide, and sulfonyluria. Among these three groups, the utilization of insulins and sulfonylurias, which had relatively cheap cost per prescription compared to the biguanide group, was fairly stable. On other hand, an increase in the number of prescriptions of the biguanide group, which contained Glucophage® having high cost per prescription, was found. Another interesting therapeutic category was the thiazolidinedione, which had very high cost per prescription. Even though Rezulin®, which was a first member of this group, was withdrawn from the market due to its toxicity, Actos® and Avandia®, which were two new members in this group, also had expensive cost per prescription and had been growing after their introductory year. This result indicated these therapeutic categories should be monitored closely to potentially reduce the drug ingredient cost.

The prescription drug ingredient cost change can be examined by various approaches. Different approaches shed light on different angles of the drug ingredient cost change. The first step of analyses was intended to explore and explain the general picture of the prescription drug ingredient costs across the study periods. Next, the second step was the decomposition analysis, which was primarily designed to apply the economic theory of index numbers to estimate the relative magnitude of the effects of inflation, prescription size, utilization, and product mix on the prescription drug ingredient cost change.

Discussion of Decomposition Analysis Results

Index Selection

This study applied the economic theory of index numbers introduced in various energy studies to the step of decomposition. Ang and Lee (1994) concluded that there were infinite numbers of methods using indexes for decomposition analysis. There was no single standard decomposition method. However, it was not practical to try all possible methods. Since this study was the first research that applied the theory of index numbers to decompose the effects on drug ingredient cost changes, the most often used indexes; Laspeyres and Torqvist discrete approximation to the Divisia indexes, representing either additive or multiplicative approaches were included. The refined Divisia index, which was the most recent index approach introduced in 1997 by Ang and Choi to the decomposition analysis, also was used in the study because it was claimed as a perfect decomposition that contained no residuals.

In Table 4.16, using either an additive or multiplicative approach did not greatly affect the relative magnitude of all effects in each period. All indexes for each effect in each period were close and had the same direction, except when they barely changed from one year to another. Therefore, it was not really critical in these particular data which index should be used. However, the studies in energy intensity decomposition research suggested that the residual term in both Laspeyres and Torqvist discrete approximation to the Divisia indexes tended to defeat the purpose of identifying the extent of each component in decomposition analysis (Ang 1994). In this case, the refined Divisia index method, which contained no residual, was therefore a preferred tool. Zhang and Ang (2001) also proved the refined Divisia index approach provided more robust results. In other words, when the amplitude of variations in the explanatory factors increased, the logarithmic terms in the refined Divisia index formulae gave more stable decomposition results.

The result from Table 4.16 was an example to confirm that the refined Divisia index could be used as a preferred method in this study. Since the percentage change of total cost PMPY varied in terms of both magnitude and direction across the periods, the Laspeyres and Torqvist approximation to the Divisia indexes contained relatively high amounts of residuals, which was not easy to interpret. An interesting result was that when the total cost PMPY change was relatively high in the first period, even though the indexes were close and consistent, the disparity among three indexes was high, compared to other periods. There were at least two reasons for this result. First, since the higher total cost PMPY change was an outcome of larger explanatory effects, then the interaction terms among those effects were potentially high, which created unexplained residuals. Second, the Laspeyres index did not have the logarithmic terms in the formula, thus it tended to give unstable results that created overlap among effects and made the degree of cancellation among all effects larger when they were added up to give the total change (Zhang and Ang 2001).

In conclusion, the study results agreed with the most recent previous research about energy factor decomposition. The refined Divisia index was a preferred index method for the decomposition analysis because it contained no residuals and was more robust. Therefore, it was selected to generally show the relative magnitude of the effects of inflation, prescription size, utilization, and product mix on the drug ingredient cost change.

Decomposition

The index results of decomposing the cost per member per year of the ongoing products were presented in Table 4.16. Even though methods used in the Express Scripts reports were different from this study, they provided similar factors influencing prescription drug ingredient cost change. Therefore, the Express Scripts reports were used as a benchmark to discuss the results from the decomposition analysis. Inflation was the only effect that was consistently positive with relatively high magnitude (between five to seven percent increase) across all study periods. This result was consistent with previous study series by Express Scripts (between four to seven percent increase). Interestingly, another consistency found was that Glucophage® 500 mg and Humulin® N 100U/ML, which were heavily used across the periods, had high percentages of unit price change. This could be a reason explaining a high magnitude of inflation in this drug group.

The index showed that the prescription size effect increased about three and four percent in the first two periods, then slightly increased and decreased in the third and last periods, respectively. Even though the magnitude of change was not close to the result from the study series by Express Script, their trends were consistent. The relative magnitude of the prescription size change effect was very moderate across the study periods, compared to other effects. After reviewing the data, one reason for this result was because of the relatively high decrease in prescription size of the multiple-source innovator products, such as Humulin® N, which also had high volume.

The product mix effect had a negative effect in the second period and a sizeable negative effect in the last period. It was the most fluctuating effect in terms of direction, compared to others, across the periods. Since the product mix effect indicated the distribution of the utilization of more or less expensive products, the positive product mix effect could occur from either the increase in utilization of more expensive products or the decrease in utilization of less expensive products, while the negative product mix effect could be attributable to either the increase in utilization of less expensive products or the decrease in utilization of more expensive products. Neither trend nor magnitude was consistent with Express Scripts' studies. Express Scripts reported a positive magnitude of product mix in the same periods. This result could be explained by the fact that the product mix effect depended on the distribution of products utilized by patients. The patients in this study were continuous anti-diabetic drug users, while the Express Script also included new diagnosed diabetes patients. Therefore the degree of product mix effect was likely positive if the new diagnosed diabetes patients tended to use more expensive products, such as the single-source ongoing products. In other words, the product mix effect in the Express Script also included the effect from new diagnosed patient mix, which was not the case in this study.

The product mix results were more complicated than other effects. It could not be explained by only a single dimension, but it depended on the overall distribution of the utilization of more and less expensive ongoing products. Based on the numbers of prescription data, the product mix effect result in the first period could be explained by some patients either switching to or using more single-source ongoing products, which were more expensive, thus an increased product mix effect. Even though a similar trend occurred in the ongoing product group in the second period, some patients might switch to Rezulin®, which was categorized as new entity in this period, therefore the effect from the decrease in the multiple-source innovator ongoing products utilization was not offset much by the increase in use of the single-source ongoing products. Also, the multiple-source generic products, which were cheaper, were highly used. Therefore, the product mix effect within the ongoing products became negative in the second period. Rezulin® was then incorporated into the single-source ongoing product group in the third period and the product mix effect turned to be positive as occurred in the first period. However, the changes in number of prescriptions for both multiple-source innovator and generic products were relatively low, compared to the second period. After combining the effects from all subgroups, the product mix effect was relatively small in the third period. Finally, the product mix effect was considerably negative in the last period because Rezulin® was withdrawn from the market.

The utilization effect was consistently positive, except for the last period. The magnitude was relatively high in the first and third periods, compared to the second and fourth periods. Similar to the effect of product mix change, this could be explained by the effect of Rezulin®. Since Rezulin® was introduced in the second year, some patients might switch to use the new entity. Therefore, the utilization effect in the ongoing products in the second period became milder than in the first period. Also, after Rezulin® was removed from the market in the last period, the utilization effect dramatically decreased.

The effect from the new ongoing products that were just launched within five years before each study period was summarized in Table 4.18. Interestingly, the new ongoing products primarily helped raise the product mix and utilization effects for all of the first three periods. The inflation effect of the overall ongoing products was inconsistently affected by the impact from the new ongoing products. One reason for this result was that the new ongoing products were relatively new and their patents were still active, their prices were already high, compared to others. As long as the patients tended to switch to or use more expensive products, which were the new ongoing products in this case, the manufacturers would still be able to gain more revenue. This was the product mix effect, which was not as easily observed as the inflation effect. If high prescription drug expenditures occurred in any health plan and the plan manager or policy maker tried to control only the inflation effect, it might partially help lowering the expenditures, but not completely.

Table 4.19 summarized all components of the total ingredient cost PMPY across the study periods. Two major components influencing the total ingredient cost PMPY were the ongoing products and new entities. While the largest influence in the first and third periods was the ongoing products, the new entities were the highest share in the second and last periods. For the first period, this could be explained by the fact that a new entity, Rezulin®, was just introduced. It required introductory time. Next, it dramatically affected the total cost PMPY in the second period. After Rezulin® was identified as an ongoing product in the third period, it then boosted the impact of the ongoing product group on the total cost PMPY. Even though Actos® and Avandia® were introduced in the third period, they also required an introductory period and hence their effect was small in the third period. Finally, Rezulin® was removed from the market in the last period. This decreased the effect of the ongoing products on total cost PMPY in this period, while Actos® and Avandia® became more popular and highly influenced the total cost PMPY.

Limitations

The study was a first research formally applying the economic theory of index numbers to decompose the effects influencing prescription drug ingredient cost changes. Previously, the index number approach was used in energy studies. The approach has been continuously improved, and there does not exist a standard decomposition method yet. To validate the tool, data from various sources are needed. However, the main goal of the study was to estimate the relative magnitude of the effects influencing prescription drug ingredient cost change, and it was not intended to completely model the ingredient cost changes. Therefore, the study results are still valuable.

Also, since the study was restricted to only one HMO setting, the results cannot be generalized to other settings. Only one HMO was chosen because the objective of this study was to empirically demonstrate the effects of inflation, prescription size, product mix, and utilization on the prescription drug ingredient costs. It is possible that there may be different results in different settings. However, the method developed in this study should be able to be used to analyze the effects in other settings.

Another limitation was that only one therapeutic group was studied. As mentioned in the methodology chapter, anti-diabetic drugs had some characteristics, which were interesting to be analyzed as an empirical example. If other therapeutic groups were used, some analyses may need to be adjusted.

Another limitation was in the issue of tracking price changes over the periods. The study methods focused only on annual changes. Some products had price changes two or three times a year. Thus these movements were invisible in this study. However, the annual changes were sufficient to track the effects of price on the drug ingredient costs, and it was convenient to analyze and compare among all products.

Another limitation arises from a population aging effect. Since the study controlled the enrollee mix effect by using claims data from the continuous enrollees, aging of the patients during the period being examined would have an impact on the ingredient cost increases, assuming older patients might tend to have higher drug utilization. However, Merlis (2000) estimated the aging effect should be only about one percent PMPY of the spending increase, which was relatively small, compared to the total changes PMPY in this study.

CHAPTER 6

CONCLUSIONS

The main goal of this study was to estimate the relative magnitude of price, prescription size, utilization, and product mix within prescription claims experienced by an HMO. Claims data for 37,470 prescriptions of anti-diabetic drugs in five consecutive years (four two-year periods) were analyzed. They were divided into four main groups, which were ongoing products, adopted products, abandoned products and new entities. Except for the new entities, they were categorized into three groups, based on types of product sources. They were single-source, multiple-source innovator, and multiple-source generic products. General descriptive information of the database, and decomposition of anti-diabetic drug ingredient costs using the theory of index numbers were presented.

The total drug ingredient costs, and numbers of prescriptions increased across the study years. While the numbers of prescriptions increased at inconsistent rate, the rate of increase in the total drug ingredient costs diminished across the study periods. Since the number of diabetes patients was fixed, there was no population mix effect in the study. The cost of ongoing products was the major part of total drug ingredient cost. Among those ongoing products, the ingredient cost of single-source products was the highest percentage share in the last two periods, while the multiple-source innovator ingredient cost was the highest in the first two periods.

The average cost per prescription, average unit price, average prescription size, and number of prescriptions across the product groups and study periods were identified. Across the ongoing products, which had large impact on the prescription ingredient cost, the single-source products were highly used, and they had more expensive average cost per prescription than the multiple-source products. Certainly, this indicated that not only price but also product mix affected prescription drug ingredient costs. Interestingly, the average unit price of the single-source ongoing products was lower than the multiple-source innovator ongoing product's unit price. One of the reasons might be that the number of units used per day across the product groups was not appropriately comparable. The average cost per day and number of days supply were then examined. The average cost per day of the single-source products became more expensive in the last two periods, which was consistent with their total ingredient cost results.

The adopted and abandoned products played minor roles on the total ingredient costs in all periods. Their effects from price and quantity used were inferior to other groups. The new entities had very unique characteristics across the study periods. They had dramatically high average cost per prescription because of their high unit prices. After their introductory years, the growth in the utilization of the new entities was found to be very high. They had an important role in almost all periods. After Rezulin® was introduced in 1997, it increased the total cost per patient per year by 16 percent in the first period, and continued growing in the second period for another 17 percent. Even though Rezulin® was withdrawn from the market in year 2000, other products that were members in the same therapeutic group, Actos® and Avandia® which were launched in 1999, raised the total ingredient cost per patient per year by about 21 percent. This effect from the new entities was stronger than the decreasing effect of the ongoing product cost in the last period.

Strength mix is another kind of product mix. There were some products, where more than one strength was available, and that were mixed by higher cost strength. The strength mix effect varied across the periods. Therapeutic mix is the utilization of more or less expensive drugs within a therapy class, which is anti-ulcer agent in this study. The numbers of prescriptions for insulin, biguanide, and sulfonyluria indicated that they had major impact in the anti-diabetic drug group. The utilization of insulin and sulfonyluria products likely remained unchanged. They had relatively cheap cost per prescription compared to the biguanide group. An increase in the number of prescriptions in the biguanide group, which contained Glucophage®, having high a cost per prescription, was found. A relatively new therapeutic group, the thiazolidinediones, had very high cost per prescription and started growing since 1997. Rezulin®, which was the first member of this group, was withdrawn from the market due to its toxicity. Actos® and Avandia®, two new members in this group, also had expensive cost per prescription and had been growing after their introductory year. This mix had a large impact on the increase in drug ingredient costs.

The Laspeyres index, Tornqvist discrete approximation to the Divisia index, and refined Divisia index were used to decompose the cost per member per year of the ongoing products. The overall results showed that even though the magnitudes of all effects were not exactly the same, they were close and had similar relative trends for all methods used. In other words, both additive and multiplicative approaches offered similar trends of all effects' movements. The refined Divisia index was chosen to present the summary of the decomposition of effects for the ongoing products since it contained no residual and it was proved to be more robust for decomposition analysis (Zhang and Ang 2001). The relative magnitude of all effects varied across studied periods. The inflation and utilization change effects had major impact in the first and third periods. Inflation was the only effect that was consistently positive (between 5.5 to 7 percent increase across all study periods). The effects of prescription size and utilization changes were consistently positive, except for the last period. The product mix effect had a negative effect in the second period and a sizeable negative effect in the last period. Even though the magnitude of the product mix effect was not high, it was considered to be relatively less stable than other effects across the periods. After the effects from the new ongoing products were examined, the product mix became more important than the inflation effect. In other words, the mix of the product utilization was highly distributed toward the new ongoing products, which were more expensive than the old ongoing products.

Implications

Compared to the previous studies, several advantages were gained from this study method. For those studies (Barents Group 1999, Dubois et al. 2000, Merck-Medco 2000, and Express Scripts 2001), which did not show how to calculate the magnitude of the effects influencing the drug ingredient cost, this study filled this gap by showing all formulas that were used to calculate the relative magnitude of all effects. The decompositions of factors affecting prescription drug ingredient cost changes were presented. The methods used in this study provided an easy interpretation because the results were presented in terms of indexes, which have been used widely. This study separated the inflation and product mix effects, which were combined into one effect in several previous studies (Barents Group 1999, Dubois et al. 2000, Merck-Medco 2000, and Chernew et al. 2001). Express Scripts used generic chemical entities as the unit of analysis since 1993, therefore the effect from different prices between brand name and generic name products was not captured. Certainly, based on their analyses, the product mix effect did not account for the distribution of utilization of brand name and generic name products. Only in the most recent two years, Express Scripts also provided the price change of brand name and generic name products separately. However, it was not clear that the method for the overall inflation effect had been changed yet. Since this study analyzed the data at the NDC number level, it clearly solved this problem because the brand name and generic name products were separated by NDC numbers.

The results of this study have a variety of policy implications. From the main goal of the study, which was to estimate the effects of inflation, prescription size, utilization, and product mix on the prescription drug ingredient cost; several approaches were developed. Health care administrators or policy makers can apply the tools to carefully examine the cost of prescription drugs within their programs. The major factors of increases in the prescription drug ingredient costs will be pointed out, and then policies or cost containment strategies can be designed to provide means to monitor highly used and expensive products.

At the same time, the manufacturers can use the information of price, utilization, prescription size, and product mix effects on the drug ingredient costs in their marketing plan such as setting appropriate product prices. For instance, the manufacturers may want their products' prices to increase properly with their products' utilization, and other competitive products' prices and quantities used.

This study also may have some impact on health care providers, if they want to help to control drug ingredient costs for their firms or for their own benefits, in case there is any incentive from lowering cost per prescription drugs.

Certainly, assuming the tools developed in this study help in making efficient policy and reducing prescription drug costs, all benefits from understanding the prescription drug ingredient cost changes eventually will accrue to the patients, who may not need to suffer from higher premiums resulting as the consequence of high prescription drug expenditures.

Future Research

Some limitations may be improved by future research. For instance, the tools developed for tracking the inflation, prescription size, utilization, and product mix effects on the prescription drug ingredient in the study were tested with data from only one HMO and one specific drug group. Future research could examine the effects of inflation, prescription size, utilization, and product mix with more data in order to confirm or study the application of the method developed.

Since this study subsequently applied the theory of index numbers from the energy studies that recently were ongoing studies, any concerns from those studies should be followed and examined by using prescription drug ingredient cost data. For example, this study focused on time series analysis, which included a series of data from several consecutive years. The changes of the ingredient costs from one year to another were likely smaller, compared to a study using periodwise data such as an analysis of data from only the first and fifth years. Different indexes may respond differently to large change in the periodwise study.

This study was the first research formally applying and clearly presenting the theory of index numbers to decompose the effects of inflation, prescription size, utilization, and product mix on the prescription drug ingredient costs. As a next step, the tools should be applied to study the prescription drug ingredient cost growth in various perspectives. For instance, it can be used to compare the prescription drug ingredient cost growth across the different types of prescription drug coverage. It can be used to study the effects or performance of cost control strategies on the inflation, prescription size, utilization, and product mix across health plans.

It can be used to decompose and compare the effects on the prescription drug ingredient cost growth across various patients' socio-demographic variables such as age groups. It also can be used to study the effects on the prescription drug ingredient cost growth across drugs' variables such as chronic versus acute therapeutic drug categories. Another possible future research is timing of inflation, prescription size, utilization, and product mix effects on the prescription ingredient cost. A pricing strategy continues over the life of a drug product, since the product is likely to face competition from similar or generic products over time. The patent expiration is an important indicator of competitive time. Future research may examine the effects of inflation, prescription size, utilization, and product mix on the prescription ingredient costs before and after patent expiration. This kind of study may provide some information to policy makers to be aware of the dynamic of the effects of inflation, prescription size, utilization, and product mix during patent expiration time of expensive products.

An interesting point for future research is the manufacturers' approach. Since the study examined the final result of product prices only when the products' are priced, future research is necessary to examine all costs from manufacturers' perspective, such as cost of research and development, and cost of advertising because they ultimately affect drug ingredient costs.

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APPENDIX A

Examples of the Calculation of Effects from Each Product Group

Calculations for the first and second periods were chosen to be examples. Since the number of enrollees was fixed, the results from either Table 4.4 or 4.6 can be used to provide the examples.

From Table 4.4, the ingredient costs across the product groups for the first period

	1996-1997		1997-1998	
Ongoing Products	161,457	199,872	203,694	217,738
Adopted Products	-	5,779	-	3,710
Abandoned Products	2,694	-	1,957	-
New Entities	-	26,500	26,500	68,831
Total	164,151	232,151	232,151	290,279

<u>1996-1997</u>:

Change of the ongoing product cost = (199,872 – 161,457) /164,151 = 0.2340 = 23.40%

Effect from adopted and abandoned products = (5,779 – 2,694)/164,151= 0.1879 = 1.88%

Effect from new entities = 26,500/164,151= 0.1614 = 16.14%

Total change = 232,151/164,151 = 1.4143 = 41.43%

<u>1997-1998</u>:

Change of the ongoing product cost = (217,738 – 203,694) /232,151 = 0.0605 = 6.05%

Effect from adopted and abandoned products = (3,710 – 1,957)/232,151 = 0.0076

= 0.76%

Effect from new entities = (68,831 – 26,500)/232,151 = 0.1823= 18.23%

Total change = 290,279/232,151= 1.2504 = 25.04%